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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/041,856	SLAUGENHAUPT ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: sequence alignment between SEQ ID NO: 86 and Accession No. ACD13384 and ACF6748.

DETAILED ACTION

1. This action is in response to the amendments filed 9/14/05 and 6/1/05. Applicant's arguments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. This action is made final.

Priority

2. It is noted that a claim as a whole is assigned an effective filing date (rather than the subject matter within a claim being assigned individual effective filing dates). Claims 44-53, 55-62, 64, 66-68, 70-74 encompass the full length sequence of SEQ ID NO: 1 and primers from any region of SEQ ID NO: 1. These claims are not entitled to priority to provisional application 60/260,080. Provisional application 60/260,080 provides a transmission letter stating that 56 sheets of drawings were filed. However, this application was not filed with a complete set of drawings. While Figure 6 states that the recited sequence is of a length of 66476 nucleotides, the drawing ends at nucleotide 53,050. Accordingly, the provisional application does not provide support for the presently claimed nucleic acids of SEQ ID NO: 1 (having a length of 66,476 nucleotides) or for primers that consist of sequences from the regions of nucleotides 53,051-66,476 of SEQ ID NO: 1. Thereby, these claims are not entitled to the priority of the provisional application and are entitled to the filing date of January 7, 2002. Additionally, claims 51-60, and 70-75 are not entitled to the filing date of provisional application '080 because this application does not appear to provide support for the concept of nucleic acids consisting of nucleotides 311-4,309 of SEQ ID NO: 2, nucleotides 2,441-2,514 of SEQ ID NO: 2, or SEQ ID NO: 89.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that a complete Figure 6 was filed in the provisional application showing all 66,476 nucleotides of SEQ ID NO: 1. However, no evidence has been filled to support this allegation. In the absence of evidence establishing that a complete Figure 6 was filed in the provisional application, it is maintained that provisional application '080 does not provide support for the full length 66,476 nucleotide sequence of SEQ ID NO: 1.

The response also states that the specification as original filed and the '080 application provide support for location of exon 20 between nucleotides 2,441 and 2,514 of SEQ ID NO: 2. In support of this argument, applicants point to the teachings in the specification of the length of exon 20 as being 74 bp and the teachings that intron 20 is 3' to exon 20 and that exon 20 ends 6 residues previous "to the FD1 mutation." It is stated that "Once exon 20 is identified in the IKAP genomic sequence in Figure 6, the corresponding sequence could be identified on the IKAP cDNA." However, the response does not clearly indicate how the teachings in the specification of the location of exon 20 provide support for the concept of a specific oligonucleotide consisting of or comprising the 10 nucleotides of SEQ ID NO: 89 or oligonucleotides consisting of nucleotides 311-4,309 of SEQ ID NO: 2 or any nucleic acid which detects exon 19 directly attached to exon 21.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS AND SPECIFICATION:

Specification

3. The amendment filed September 8, 2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The specification as originally filed does not provide basis for newly added SEQ ID NO: 89. The response states that support for this amendment may be found in provisional application 60/260,080 at pages 6 and 13 and Figure 2C. The cited portions of '080 teach the occurrence of a T to C point mutation at bp 6 of intron 20, resulting in the skipping of exon 20 in the mRNA of the FD gene. However, the '080 application does not teach the particular nucleotide sequence of SEQ ID NO: 89.

The response also states that using the information that there is a T to C change at residue of intron 20, the disclosure in Figure 1 that intron 20 is 3' to exon 20, the teachings that exon 20 consists of 74 bp and the teachings of the sequence of exon 20 in Figure 6, one could determine that exon 20 is between nucleotides 2,441 and 2,514 of the IKAP cDNA and thereby arrive at the exon 19/21 junction of SEQ ID NO: 89. However, these teachings do not lead one to a nucleic acid consisting of the specific 10 nucleotide fragment containing sequences from exon 19 and 21. The response does not point to any specific teachings in the specific which provide support for a nucleic acid consist of 10 nucleotides of the splice junction between exons 19 and 21. Accordingly, the specification as originally filed does not provide basis for a nucleic acid consisting of SEQ ID NO: 89.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

4. Claims 51-60, 70-73 and 75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A. The specification as originally filed does not provide basis for the recitation in newly added claims 53, 72 and 73 of a nucleic acid or probe consisting of SEQ ID NO: 89 or nucleic acid or probe comprising SEQ ID NO: 89, wherein said SEQ ID NO: 89 is flanked by nucleotides of any length and identity. As discussed above, while the '080 teaches the occurrence of a T to C point mutation at bp 6 of intron 20, resulting in the skipping of exon 20 in the mRNA of the FD gene, this application and the present application as originally filed do not teach the particular nucleotide sequence of SEQ ID NO: 89. Further, the teachings in the '080 application of the T to C mutation in intron 20, the size of exon 20 and the genomic DNA sequence of Figure 6 does not provide support for the specific concept of a nucleic acid consisting of SEQ ID NO: 89 or any nucleic acid comprising SEQ ID NO: 89.

B. Further, the specification as originally filed does not appear to provide support for the recitation in claims 51-53, 70-73 of a probe or nucleic acid which detects a deletion of exon 20 wherein exon 20 consists of nucleotides 2,441-2,514 of SEQ ID NO: 2. As discussed above, the teachings in the specification of a T to C point mutation at residue 6 of exon 20, together with the teachings that exon 20 consists of 74 bp, does

not provide support for a particular nucleic acid consisting of exon 20 and particularly consisting of nucleotides 2,441-2,514 of SEQ ID NO: 2. The disclosure in the specification of a full length nucleic acid does not provide basis for the concept of particular fragments of nucleic acids consisting of individual exons or comprising individual exons.

C. The specification as originally filed does not appear to provide support for the recitation in claims 54-60 and 75 of a nucleic acid consisting of nucleotides 311-4,309 of SEQ ID NO: 2. The response points to pages 29 and 31 of the specification as providing support for this amendment. However, neither the cited sections, nor other portions of the specification, provide support for the concept of a nucleic acid that begins at nucleotide 311 and terminates at nucleotide 4,309 of SEQ ID NO: 2.

5. Claims 44-49, 51-53, 55-62, 64, 66-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acids comprising SEQ ID NO: 1 or 2 or nucleic acids consisting of SEQ ID NO: 82-86, does not reasonably provide enablement for nucleic acids comprising position 34,201 or 33,714 of SEQ ID NO: 1 wherein there is a cytosine at this position, or comprising position 2,397 of SEQ ID NO: 2 wherein there is a cytosine at this position, or comprising SEQ ID NO: 85, 86 or 89, wherein each of the nucleic acids is flanked by nucleotides of any identity and length. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the Claims:

The claims are broadly drawn to (i) nucleic acids comprising position 34,201 of SEQ ID NO: 1 wherein thymine is a cytosine; (ii) nucleic acids comprising the 15 mer of SEQ ID NO: 85; (iii) nucleic acids comprising position 33,714 of SEQ ID NO: 1 wherein guanine is a cytosine; (iv) nucleic acids comprising the 15 mer of SEQ ID NO: 86; (v) nucleic acids comprising position 2,397 of SEQ ID NO: 2 wherein guanine is a cytosine; (vi) nucleic acids that detect a deletion of exon 20 in IKAP cDNA; (vii) nucleic acids comprising the 10 mer of SEQ ID NO: 89. Because of the use of the term "comprising", such nucleic acid molecules may include additional flanking sequences, including intron sequences and 5' and 3' untranslated sequences. The claims do not set forth the number or identity of nucleotides flanking the recited nucleic acid fragments. Accordingly, the claims encompass nucleic acids which comprise the recited 1, 10 or 15 nucleotides but which share any level of sequence identity with SEQ ID NO: 1 and 2 (e.g., 80%, 60%, 20% etc). The claims thereby encompass naturally and non-naturally occurring allelic, mutant and splice variants and homologues of SEQ ID NO: 3. The claims also do not identify the mutation that is to be detected by the oligonucleotide.

Rather, the claims broadly recite that the oligonucleotide has the property of being useful for "detecting the presence of a mutation associated with Familial Dysautonomia." The claims do not set forth the gene in which the mutation is to be detected or the location or identity of the mutation.

Nature of the Invention:

The claims are drawn to isolated nucleic acids comprising portions of the IKAP cDNA and genomic DNA. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F. 3d 1316, 1330 (Fed Cir. 2001).

State of the Art:

The specification teaches the complete cDNA sequence (SEQ ID NO: 2) and genomic sequence (SEQ ID NO: 1) of the IKAP gene. The IKBKAP genomic DNA spans 66,479 nucleotides. The specification further teaches two mutations in the IKBKAP gene: a) the "FD1" mutation located at bp6 within intron 20, wherein a thymine is replaced by a cytosine; and b) the "FD2" located at position 2396 (bp73 of exon 19) wherein a guanine is replaced by a cytosine, leading to a missense arginine to proline mutation at amino acid position 696. The specification and prior art do not teach any additional mutations in the IKBKAP gene and particularly does not teach any additional IKBKAP mutations associated with FD. Further, the specification and prior art do not teach any homologues or splice variants of the IKAP gene.

The Predictability or Unpredictability of the Art and Degree of Experimentation:

The prior art acknowledges the unpredictability in modifying the nucleotide sequence of a gene. Modification of even a single nucleotide within a coding or non-coding sequence can significantly alter the functional properties of that gene and protein encoded thereby. The specification does not provide any information as to regions of SEQ ID NO: 1 and 2 which are critical for functional activity and for maintaining the three dimensional structure of the encoded protein in order to allow for the encoded protein to be associated with the occurrence of FD. There is no disclosure in the specification as to how nucleic acids which share only one nucleotide in common with the IKAP gene can be used to detect mutations in the IKAP gene or to detect deletions of exon 20. There is also no disclosure as to the degree of sequence identity shared between the IKAP gene and other genes which would allow one to modify the IKAP sequences and add flanking nucleotides of any length and identity, yet still maintain the properties of a nucleic acid as useful for detecting any mutation associated with FD. Thereby, it is highly unpredictable as to how modifying sequences within SEQ ID NO: 1 and 2 will effect the overall functional properties of the resulting gene. It is also unpredictable as to how adding nucleotides of any identity or length to the terminus of fragments of 1 nucleotide of SEQ ID NO: 2, or the 10 nucleotides of SEQ ID NO: 89 or the 15 nucleotides of SEQ ID NO: 85 and 86 will effect the functional properties of the resulting nucleic acid. The additional of nucleotides of any identity to the terminus of these nucleic acids would be expected to significantly effect their functional activity. For instance, Accession No. ACD13384 discloses a nucleic acid comprising SEQ ID NO: 86 and additional flanking nucleotides wherein the nucleic acid has the activity of a p53

modifier. Similarly, Accession No. ACF67648 discloses an isolated nucleic acid comprising SEQ ID NO: 86, wherein the nucleic acid is from *Photorhabdus luminescens* and has antibacterial or antifungicidal activity. Thereby, the effect of adding nucleotides to the 3' or 5' end of fragments of the IKAP gene is highly unpredictable.

Further, the claims do not specify the identity of the gene or the mutation associated with FD that is to be detected by the oligonucleotides. The art of identifying genes associated with a disease and detecting the presence of novel mutations associated with the occurrence of disease is highly unpredictable. Knowledge of the FD1 and FD2 mutations does not lead one to any additional mutations in the IKAP gene or any other gene. There is no common structural feature linking the broadly claimed oligonucleotides which are defined only in terms of their functional properties and not in terms of their structural properties. With respect to the IKAP gene, it is unpredictable as to which residues within this gene of over 60Kb are important to the functional activity of the encoded protein and which nucleotides are variable in nature and are associated with the occurrence of FD. To identify additional genes or mutations requires extensive, trial-by-error experimentation in which researchers may be required to map genes, perform linkage analysis to determine the inheritance pattern of polymorphisms, sequence genes, identify specific mutations in the sequenced gene, analyze members of the population which have FD and individuals who do not have FD for the presence or absence of a polymorphism or mutation and try to ascertain which specific polymorphisms or mutations are associated with the occurrence of disease. Such experimentation is considered to be undue.

Amount of Direction or Guidance Provided by the Specification:

The specification does not provide any specific guidance as to how to predictably make and use nucleic acids comprising any 1, 10 or 15 nucleotide fragment of SEQ ID NO: 1 or 2 flanked by nucleotides of any length and identity. While one could generate a significantly large genus of nucleic acids in which nucleotides of any identity are added to the 5' or 3' terminus of fragments of SEQ ID NO: 1 or 2, 85, 86 or 89 or in which any number of nucleotides within SEQ ID NO: 1 and 2 are mutated via substitution, addition or deletion, and then assay each of these nucleic acids to try to determine their biological activity, such trial-by-error experimentation is considered to be undue. Providing methods for searching for additional nucleic acids and trying to determine if the resulting nucleic acid will detect an undefined mutation associated with FD is not equivalent to teaching how to make and use specific nucleic acids.

Further, the specification does not provide any specific guidance as to how to predictably identify additional mutations in the IKBKAP gene or as to how to identify additional genes containing mutations associated with FD. While methods for sequencing genes and comparing the sequence of genes from patients and control individuals are known in the art, such methods provide only the general guidelines that allow researchers to search for novel mutations. Providing methods for searching for a mutation and for additional FD-associated genes is not equivalent to teaching how to make and use specific oligonucleotides which detect specific FD mutations.

Working Examples:

Again, the specification teaches only the IKAP genomic DNA of SEQ ID NO: 1, the IKAP cDNA of SEQ ID NO: 2, the probes of SEQ ID NO: 85 and 86 and a nucleic acid spanning the exon 19/21 junction (SEQ ID NO: 89). The specification does not provide any working examples of how to predictably make and use nucleic acids comprising 1 nucleotide of SEQ ID NO: 1 or 2 for the purposes of detecting any mutation associated with FD. There is no disclosure in the specification of additional nucleic acids which contain any number or identity of nucleotides flanking the recited nucleotide, other than nucleic acids which contain the sequences of SEQ ID NO: 1 and 2.

Also, the specification teaches only 2 mutations in the IKBKAP gene, namely the FD1 and FD2 mutations, as defined on page 3 of the specification. The specification does not provide any additional examples of FD-associated mutations in the IKAP gene or in other unspecified genes.

Conclusions:

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v*

Novo Nordisk 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, the claims do not bear a reasonable correlation to the scope of enablement because the specification teaches only the full length cDNA and genomic DNA of the IKAP gene (i.e., SEQ ID NO: 2 and 1), whereas the claims encompass a significantly large genus of nucleic acids, in which the overall structural and functional properties of the nucleic acids are not clearly defined. As set forth above, in view of the unpredictability in the art, extensive experimentation would be required to make and use additional nucleic acids containing only 1 nucleotide of SEQ ID NO: 1 or 2 or only the 10 nucleotides of SEQ ID NO: 89 or the 15 nucleotides of SEQ ID NO: 85 and 86 because the specification does not provide sufficient guidance as to how to select the nucleotides which may flank the fragments and does not teach a predictable means for determining which of the resulting nucleic acids will have the functional property of being capable of detecting a mutation associated with FD. Additionally, the claims do not bear a reasonable correlation to the scope of enablement because the specification teaches only 2 members of the broadly claimed genus of oligonucleotides which detect any mutation in any gene associated with FD and oligonucleotides which hybridize to sequences at any distance to a region flanking a FD-associated mutation. In view of the unpredictability in the art, extensive experimentation would be required to identify additional IKAP mutations and mutations in other genes associated with FD. Accordingly, although the level of skill in the art of molecular biology is high, given the lack of disclosure in the specification and in the prior

art, it would require undue experimentation for one of skill in the art to make and use the broadly claimed invention.

6. Claims 44-49, 51-53, 55-62, 64, and 66-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims as broadly written encompass isolated nucleic acids comprising a cytosine at position 34,201 of SEQ ID NO: 1 or comprising a cytosine at position 33,714 of SEQ ID NO: 1 or a cytosine at position 2,397 of SEQ ID NO: 2. The claims do not define the overall length of the molecule or the nucleotides flanking the cytosine. The claims also encompass nucleic acids comprising the 15 nucleotides of SEQ ID NO: 85 and 86 or the 10 nucleotides of SEQ ID NO: 89. Again, the claims do not define the flanking nucleotides in terms of their number or identity. Claims 51 and 52 are also broadly drawn to any nucleic acid molecule that has the property of being useful for diagnosing FD by detecting a deletion of exon 20. These claims do not define the nucleotide sequence of the nucleic acid or the length of the nucleic acid. Further, claims 61, 62, 64, 66, 67, 68 encompass nucleic acids that amplify the FD1 and FD2 mutations. The nucleic acids are not limited in terms of their nucleotide sequence, length or specificity of hybridization or amplification.

Nucleic acids which comprise or consist of SEQ ID NO: 1 or 2 and nucleic acids consisting of SEQ ID NO: 85 and 86 meet the written description requirements.

However, the specification does not provide an adequate written description of the claimed genus of nucleic acids that comprise a cytosine flanking by any number and identity of additional nucleotides.

The specification teaches 2 mutations in the IKBKAP gene: a) the "FD1" mutation located at bp6 within intron 20, wherein a thymine is replaced by a cytosine; and b) the "FD2" located at position 2396 (bp73 of exon 19) wherein a guanine is replaced by a cytosine, leading to a missense arginine to proline mutation at amino acid position 696. The specification further teaches the complete cDNA sequence (SEQ ID NO: 2) and genomic sequence (SEQ ID NO: 1) of the IKBKAP gene. The IKBKAP genomic DNA spans 66,479 nucleotides.

The claims do not clearly define the nucleic acids in terms of their overall structure. A wide variety of nucleic acids comprise a cytosine, wherein such nucleic acids have significantly different functional activities from the nucleic acids of SEQ ID NO: 1 and 2. For instance, Accession No. ACD13384 discloses a nucleic acid comprising SEQ ID NO: 86 and additional flanking nucleotides wherein the nucleic acid has the activity of a p53 modifier. Similarly, Accession No. ACF67648 discloses an isolated nucleic acid comprising SEQ ID NO: 86, wherein the nucleic acid is from *Photorhabdus luminescens* and has antibacterial or antifungicidal activity. Accordingly, the claims are inclusive of nucleic acid molecules which have distinct biological activities from the disclosed nucleic acids of SEQ ID NO: 1 and 2.

Additionally, the claims do not set forth the number or identity of nucleotides flanking the recited nucleic acid fragments. Accordingly, the claims encompass nucleic

acids which comprise the recited cytosine or 15 or 10 mer fragment of SEQ ID NO: 85, 86 and 89 but which share any overall level of sequence identity with SEQ ID NO: 1 and 2 (e.g., 80%, 60%, 10% etc). The claims thereby encompass naturally and non-naturally variants of the FD gene, wherein the variants may include nucleotide substitutions, additions, deletions, translocations and truncations and splice variants.

The general knowledge in the art concerning homologues, mutants, allelic and splice variants does not provide any indication of how modification of the sequence of SEQ ID NO: 1 and 2 will effect the functional properties of SEQ ID NO: 1 and 2. The structure and function of one molecule does not provide guidance as to the structure and function of other molecules. Therefore, the description of the genomic sequence of SEQ ID NO: 1 and the cDNA sequence of SEQ ID NO: 2 is not representative of a genus of homologues, splice, mutant and allelic variants of SEQ ID NO: 1 and 2 having unspecified functional activities different from that of SEQ ID NO: 1 and 2. A general statement in the specification of a desire to obtain gene sequences, homologues from other species, mutated species, and polymorphic sequences is not equivalent to providing a clear and complete description of specific sequences which fall within the claimed genus of nucleic acids.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its

enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". The limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art that Applicants were in possession of the claimed homologues, mutants, allelic and splice variants of SEQ ID NO: 1 and 2. Therefore, the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 75 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 75 is indefinite over the recitation of "wherein said DNA molecule consisting of a nucleic acid sequence selected from the group consisting of" because

this phrase lacks proper antecedent basis. While the claim previously refers to a DNA molecule encoding a mutant IKAP polypeptide, the claim does not previously refer to a DNA molecule consisting of one of the recited nucleic acid sequences.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 44-75 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13, 29-35 and 43 of copending Application No. 11/073,203. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '203 are both drawn to isolated nucleic acids comprising a cytosine at position 34,201 of SEQ ID NO: 2, a cytosine at position 33,714 of SEQ ID NO: 1.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It is noted that the above new grounds of rejection was necessitated by applicant's filing of a new application after the mailing of the previous Office action.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 44, 46-49, 51, 52, 55-57 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Cohen (U.S. Patent No. 5,891,719).

Cohen teaches an isolated nucleic acid encoding for IKBKAP (referred to therein as 'IKAP; see SEQ ID NO: 1). The nucleic acid of Cohen contains a guanine at nucleotide position 2087, which corresponds to position 2397 of present SEQ ID NO: 2. The nucleic acid of Cohen also comprises SEQ ID NO: 86, wherein the "S" in SEQ ID NO: 86 is a "G". It is a property of the nucleic acid of Cohen that it would be capable of detecting the FD mutation at position 2397. For example, use of the nucleic acid of Cohen in a SSCP assay would allow for the detection of a cytosine in place of a guanine at position 2397. The nucleic acid of Cohen contains a C and thereby constitutes an oligonucleotide that comprises position 34,201 wherein a thymine is replaced with a cytosine or position 33,714 wherein a guanine is replaced with a

cytosine. It is noted that the claims do not specified the length of the oligonucleotide, or the identity of nucleotides flanking the cited nucleotide. Further, as noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." In the present situation, the claim language of "for detecting the presence of a mutation associated with Familial Dysautonomia" is a statement of purpose and intended result. Accordingly, the structural properties of the product are able to stand alone and therefore the preamble limitation is not accorded patentable weight. Thereby, the claims encompass any nucleic acid comprising a cytosine or comprising position 34,201 of SEQ ID NO: 1. Accordingly, the nucleic acid of Cohen anticipates the claimed invention.

With respect to claims 55-57 and 60, Cohen (e.g., column 3 and 5) further teaches vectors and host cells, particularly mammalian host cells, comprising the IKBKAP cDNA. In particular, the reference (column 3 and 4) teaches methods for synthesizing recombinant IKBKAP using host cells transformed with IKBKAP, wherein the host cells are preferably human or other mammalian cells. Cohen (column 7-8) teaches use of the recombinant protein to identify compounds that bind to IKBKAP, which can then potentially be used for diagnostic and therapeutic applications.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Cohen teaches wildtype IKAP cDNA and does not teach a cytosine at position 2,397 of SEQ ID NO: 2. Also, it is stated that

"because the FD1 mutation is located in intron 20 of the IKAP gene, it is not present in the IKAP cDNA." Therefore, applicants conclude that the cited prior art does not disclose the FD1 mutation.

These arguments have been fully considered but are not persuasive. The claims are not limited to molecules that comprise the full length nucleic acid of SEQ ID NO: 2 and which differ from SEQ ID NO: 2 only in that they contain a cytosine in place of a quinine at nucleotide position 2,397 of SEQ ID NO: 1. Further, the claims are not limited to nucleic acids containing a full length IKAP genomic DNA containing a mutation in intron 20. Rather, the claims are very broadly drawn to any oligonucleotide that comprises position 34,201 wherein the thymine at position 34,201 is a cytosine or any oligonucleotide that comprises a cytosine at position 33,714. The claims do not define the nucleotides flanking the cytosine, or the length of the oligonucleotide. Accordingly, the claims read on any nucleic acid comprising a cytosine. Further, claim 51 is drawn to an isolated nucleic acid molecule. The intended use of the nucleic acid molecule for diagnosing FD is not given any patentable weight, for the reasons stated in the above rejection. With respect to claim 52, the claim does not require a nucleic acid in which exon 19 is directly attached to exon 21 of the IKAP cDNA. Rather, the claims encompass the wildtype cDNA which is capable of detecting a cDNA in which exon 19 is linked to exon 21 and exon 20 is deleted.

10. Claim 44, 46-49, 51, 52 and 54 are rejected under 35 U.S.C. 102(a) as being anticipated by Rubin (2002/0168656; cited in the IDS).

Rubin (page 1, column 2) discloses a cDNA encoding IKAP having GenBank Accession No. NM_003640. This cDNA is 4803 bp in length, whereas the IKBKAP cDNA of the present invention (Figure 7 and SEQ ID NO :2) is 5924bp in length. Rubin further teaches mutations in the IKBKAP wherein the first mutation is a G to C transversion at nucleotide 2390 in exon 19 of Accession No. NM_003640 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 1, column 2). The nucleic acid of Rubin also comprises SEQ ID NO: 86. The reference also teaches primers for amplifying exons 19-21 (page 1, column 2 and page 2, column 1) and PCR amplification products containing each of the above mutations. Accordingly, Rubin teaches oligonucleotides for detecting a mutation in the FD gene, wherein the oligonucleotide hybridizes to a FD mutation or to a region flanking a FD mutation.

The nucleic acid of Rubin contains a C and thereby constitutes an oligonucleotide that comprises position 34,201 wherein a thymine is replaced with a cytosine or position 33,714 wherein a guanine is replaced with a cytosine. It is noted that the claims do not specify the length of the nucleic acid, or the identity of nucleotides flanking the cited nucleotide. Further, as noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." In the present situation, the claim language of "for detecting the presence of a mutation associated with Familial Dysautonomia" is a

statement of purpose and intended result. Accordingly, the structural properties of the product are able to stand alone and the preamble limitation is not accorded patentable weight. Thereby, the claims encompass any nucleic acid comprising a cytosine at position 34,201 or 33,741 of SEQ ID NO: 1. Further, with respect to claims 51 and 52, the nucleic acids would be able to detect a nucleic acid in which exon 19 is directly attached to the nucleic acid of exon 21 because the nucleic acid can hybridize to IKKAP nucleic acids and distinguish between molecules which contain exon 20 and those which have a deletion of exon 20. With respect to claim 54, Rubin teaches the cDNA that encodes for the IKAP protein, wherein the cDNA starts at position 304 (equivalent to position 311 of SEQ ID NO: 2) and terminates at position 4302 (equivalent to position 4309 of present SEQ ID NO: 2). Accordingly, the nucleic acid of Rubin anticipates the claimed invention.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Rubin is not prior art to the claimed invention because Applicants are entitled to the filing date of January 6, 2001. However, for the reasons stated above, the claims are not limited to the subject matter that is entitled to the priority date of January 6, 2001 and thereby Rubin is prior art to the claimed invention. Further, with respect to claim 54, the response states that pages 29 and 31 of the specification provide support for this amendment, and that priority for this amendment may be found on pages 2 and 6 of the '080 application. However, the cited pages disclose SEQ ID NO: 2 and the location of the guanine to cytosine mutation. Additionally, the present specification teaches a 5.9 kb transcript. However, the cited

pages do not disclose a nucleic acid that begins at nucleotide position 311 of SEQ ID NO: 2 and ends at nucleotide position 4,309 of SEQ ID NO: 2. Therefore, it does not appear that the '080 application provides priority for this subject matter.

11. Claims 44, 46-49, 51, 52, and 54 are rejected under 35 U.S.C. 102(a) as being anticipated by Anderson (American Journal of Human Genetics (March 2001) 68: 753-758; cited in the IDS).

Anderson (page 754) discloses a cDNA encoding human IKBKAP having GenBank Accession No. NM_003640. This cDNA is 4803 bp in length, whereas the IKBKAP cDNA of the present invention (Figure 7 and SEQ ID NO :2) is 5924bp in length. Anderson further teaches mutations in the IKBKAP wherein the first mutation is a G to C transversion at nucleotide 2390 in exon 19 of Accession No. NM_003640 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 754). The nucleic acid of Anderson also comprises SEQ ID NO: 86. The reference also teaches primers for amplifying exons 19-21 (Figures 1 and 4) and PCR amplification products containing each of the above mutations. Accordingly, Anderson teaches oligonucleotides for detecting a mutation in FD, wherein the oligonucleotide hybridizes to a FD mutation or to a region flanking a FD mutation.

The nucleic acid of Anderson contains a C and thereby constitutes an oligonucleotide that comprises position 34,201 wherein a thymine is replaced with a cytosine or position 33,714 wherein a guanine is replaced with a cytosine. It is noted that the claims do not specify the length of the nucleic acid, or the identity of nucleotides flanking the cited nucleotide. Further, as noted in the MPEP 211.02, " a preamble is

generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." In the present situation, the claim language of "for detecting the presence of a mutation associated with Familial Dysautonomia" is a statement of purpose and intended result. Accordingly, the structural properties of the product are able to stand alone and the preamble limitation is not accorded patentable weight. Thereby, the claims encompass any nucleic acid comprising a cytosine at position 34,201 or 33,741 of SEQ ID NO: 1. Further, with respect to claims 51 and 52, the nucleic acids would be able to detect a nucleic acid in which exon 19 is directly attached to the nucleic acid of exon 21 because the nucleic acid can hybridize to IKKAP nucleic acids and distinguish between molecules which contain exon 20 and those which have a deletion of exon 20. With respect to claim 54, Anderson teaches the cDNA that encodes for the IKAP protein, wherein the cDNA starts at position 304 (equivalent to position 311 of SEQ ID NO: 2) and terminates at position 4302 (equivalent to position 4309 of present SEQ ID NO: 2). Accordingly, the nucleic acid of Anderson anticipates the claimed invention.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Anderson is not prior art to the claimed invention because Applicants are entitled to the filing date of January 6, 2001. However, for the reasons stated above, the claims are not limited to the subject matter that is entitled to the priority date of January 6, 2001 and thereby Anderson is prior art to the

claimed invention. Further, with respect to claim 54, the response states that pages 29 and 31 of the specification provide support for this amendment, and that priority for this amendment may be found on pages 2 and 6 of the '080 application. However, the cited pages disclose SEQ ID NO: 2 and the location of the guanine to cytosine mutation. Additionally, the present specification teaches a 5.9 kb transcript. However, the cited pages do not disclose a nucleic acid that begins at nucleotide position 311 of SEQ ID NO: 2 and ends at nucleotide position 4,309 of SEQ ID NO: 2. Therefore, it does not appear that the '080 application provides priority for this subject matter.

12. Claims 44, 46-49, 51, 52 and 54 are rejected under 35 U.S.C. 102(a) as being anticipated by Slaugenhaupt (American Journal of Human Genetics (March 2001) 68: 598-605; cited in the IDS).

Slaugenhaupt (page 600) discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). Slaugenhaupt further teaches mutations in the IKBKAP wherein the first mutation is a G to C transversion at nucleotide 2397 in exon 19, resulting in a arginine to proline missense mutation at amino acid position 696 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 602). The nucleic acid of Slaugenhaupt also comprises SEQ ID NO: 86. The reference also teaches amplification products containing the 2 mutations wherein the amplification products are generated by amplifying IKBKAP sequences using primers to exons 19 and 20/21 (page 599). Accordingly, Slaugenhaupt teaches oligonucleotides for detecting a mutation in FD, wherein the oligonucleotide hybridizes to a FD mutation.

Additionally, the nucleic acid of Slaugenhaupt contains a C and thereby constitutes an oligonucleotide that comprises position 34,201 wherein a thymine is replaced with a cytosine or position 33,714 wherein a guanine is replaced with a cytosine. It is noted that the claims do not specify the length of the nucleic acid, or the identity of nucleotides flanking the cited nucleotide. Further, as noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." In the present situation, the claim language of "for detecting the presence of a mutation associated with Familial Dysautonomia" is a statement of purpose and intended result. Accordingly, the structural properties of the product are able to stand alone and the preamble limitation is not accorded patentable weight. Thereby, the claims encompass any nucleic acid comprising a cytosine at position 34,201 or 33,741 of SEQ ID NO: 1. Further, with respect to claims 51 and 52, the nucleic acids would be able to detect a nucleic acid in which exon 19 is directly attached to the nucleic acid of exon 21 because the nucleic acid can hybridize to IKKAP nucleic acids and distinguish between molecules which contain exon 20 and those which have a deletion of exon 20. With respect to claim 54, Slaugenhaupt teaches the cDNA that encodes for the IKAP protein, wherein the cDNA starts at position 311 and terminates at position 4309. Accordingly, the nucleic acid of Slaugenhaupt anticipates the claimed invention.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Slaugenhaupt is not prior art to the claimed invention because Applicants are entitled to the filing date of January 6, 2001. However, for the reasons stated above, the claims are not limited to the subject matter that is entitled to the priority date of January 6, 2001 and thereby Slaugenhaupt is prior art to the claimed invention. Further, with respect to claim 54, the response states that pages 29 and 31 of the specification provide support for this amendment, and that priority for this amendment may be found on pages 2 and 6 of the '080 application. However, the cited pages disclose SEQ ID NO: 2 and the location of the guanine to cytosine mutation. Additionally, the present specification teaches a 5.9 kb transcript. However, the cited pages do not disclose a nucleic acid that begins at nucleotide position 311 of SEQ ID NO: 2 and ends at nucleotide position 4,309 of SEQ ID NO: 2. Therefore, it does not appear that the '080 application provides priority for this subject matter.

13. Claims 44, 46-49, 51, and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Gill et al (GenBank Accession No. AF153419, published 02 January 2001).

Gill discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). The cDNA of Gill includes nucleotide position 2397 and hybridizes with IKBKAP nucleic acids comprising the 2397 FD mutation. The nucleic acid of Gill also comprises SEQ ID NO: 86, wherein the "S" in SEQ ID NO: 86 is a "G". Accordingly, Gill teaches an oligonucleotide for detecting a mutation in FD, wherein the oligonucleotide hybridizes to a FD mutation. The nucleic acid of Gill contains a C and

thereby constitutes an oligonucleotide that comprises position 34,201 wherein a thymine is replaced with a cytosine or position 33,714 wherein a guanine is replaced with a cytosine It is noted that the claims do not specify the length of the nucleic acid, or the identity of nucleotides flanking the cited nucleotide. Further, as noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." In the present situation, the claim language of "for detecting the presence of a mutation associated with Familial Dysautonomia" is a statement of purpose and intended result. Accordingly, the structural properties of the product are able to stand alone and the preamble limitation is not accorded patentable weight. Thereby, the claims encompass any nucleic acid comprising a cytosine at position 34,201 or 33,741 of SEQ ID NO: 1. Further, with respect to claims 51 and 52, the nucleic acids would be able to detect a nucleic acid in which exon 19 is directly attached to the nucleic acid of exon 21 because the nucleic acid can hybridize to IKKAP nucleic acids and distinguish between molecules which contain exon 20 and those which have a deletion of exon 20. Accordingly, the nucleic acid of Slaugenhaupt anticipates the claimed invention.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Gill teaches wildtype IKAP cDNA and does not teach a cytosine at position 2,397 of SEQ ID NO: 2. Also, it is stated that "because the FD1 mutation is located in intron 20 of the IKAP gene, it is not present in the IKAP

cDNA." Therefore, applicants conclude that the cited prior art does not disclose the FD1 mutation.

These arguments have been fully considered but are not persuasive. The claims are not limited to molecules that comprise the full length nucleic acid of SEQ ID NO: 2 and which differ from SEQ ID NO: 2 only in that they contain a cytosine in place of a quinine at nucleotide position 2,397 of SEQ ID NO: 1. Further, the claims are not limited to nucleic acids containing a full length IKAP genomic DNA containing a mutation in intron 20. Rather, the claims are very broadly drawn to any oligonucleotide that comprises position 34,201 wherein the thymine at position 34,201 is a cytosine or any oligonucleotide that comprises a cytosine at position 33,714. The claims do not define the nucleotides flanking the cytosine, or the length of the oligonucleotide. Accordingly, the claims read on any nucleic acid comprising a cytosine. Further, claim 51 is drawn to an isolated nucleic acid molecule. The intended use of the nucleic acid molecule for diagnosing FD is not given any patentable weight, for the reasons stated in the above rejection. With respect to claim 52, the claim does not require a nucleic acid in which exon 19 is directly attached to exon 21 of the IKAP cDNA. Rather, the claims encompass the wildtype cDNA which is capable of detecting a cDNA in which exon 19 is linked to exon 21 and exon 20 is deleted.

14. Claims 44, 46-49, 51, and 52 are rejected under 35 U.S.C. 102(a) as being anticipated by Slaugenhaupt et al (GenBank Accession No. AF153419, published 28 February 2001; cited in the IDS).

Slaugenhaupt discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). In the comments section of the sequence, it is noted that a polymorphism is present at nucleotide position 2397. The cDNA of Slaugenhaupt includes nucleotide position 2397 and hybridizes with IKBKAP nucleic acids comprising the 2397 FD mutation. The nucleic acid of Slaugenhaupt also comprises SEQ ID NO: 86, wherein the "S" in SEQ ID NO: 86 is a "G". Accordingly, Slaugenhaupt teaches an oligonucleotide for detecting a mutation in FD, wherein the oligonucleotide hybridizes to a FD mutation. Additionally, the nucleic acid of Slaugenhaupt contains a C and thereby constitutes an oligonucleotide that comprises position 34,201 wherein a thymine is replaced with a cytosine or position 33,714 wherein a guanine is replaced with a cytosine. It is noted that the claims do not specify the length of the nucleic acid, or the identity of nucleotides flanking the cited nucleotide. Further, as noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." In the present situation, the claim language of "for detecting the presence of a mutation associated with Familial Dysautonomia" is a statement of purpose and intended result. Accordingly, the structural properties of the product are able to stand alone and the preamble limitation is not accorded patentable weight. Thereby, the claims encompass any nucleic acid comprising a cytosine at position 34,201 or 33,741 of SEQ ID NO: 1. Further, with

respect to claims 51 and 52, the nucleic acids would be able to detect a nucleic acid in which exon 19 is directly attached to the nucleic acid of exon 21 because the nucleic acid can hybridize to IKKAP nucleic acids and distinguish between molecules which contain exon 20 and those which have a deletion of exon 20. Accordingly, the nucleic acid of Slaugenhaupt anticipates the claimed invention.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Slaugenhaupt is not prior art to the claimed invention because Applicants are entitled to the filing date of January 6, 2001. However, for the reasons stated above, the claims are not limited to the subject matter that is entitled to the priority date of January 6, 2001 and thereby Slaugenhaupt is prior art to the claimed invention.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 61, 62, 64, 66-71, 73 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen in view of Fodor (U.S. Patent NO. 5,968,740).

Cohen teaches an isolated nucleic acid encoding for IKBKAP (referred to therein as 'IKAP'; see SEQ ID NO: 1). The nucleic acid of Cohen contains a guanine at nucleotide position 2087, which corresponds to position 2397 of present SEQ ID NO: 2. It is a property of the nucleic acid of Cohen that it would be capable of detecting the FD mutation at position 2397. For example, use of the nucleic acid of Cohen in a SSCP assay would allow for the detection of a cytosine in place of a guanine at position 2397. Additionally, Cohen teaches detecting IKBKAP nucleic acids by first amplifying the nucleic acids by PCR and then detecting the amplified nucleic acids using hybridization probes (columns 5 and 6). Cohen also exemplifies nucleic acids useful as primers or probes (see, e.g., Table 3). With respect to claims 62 and 64, the specification does not define the term "consisting essentially of" as it relates to the length of a nucleic acid, and thereby this phrase has been interpreted to included lengths comprising 399 or 500 nucleotides and lengths less than 399 and 500 nucleotides. With respect to claims 66-68, the primers of Cohen are able to amplify a region that contains a G or T (i.e., position 33,741 or 34,201 of SEQ ID NO: 1 and position 2,397 of SEQ ID NO: 2). With respect to claim 69, the nucleic acid of Cohen comprises SEQ ID NO: 86 wherein "S" is a "G." With respect to claims 70 and 71, the nucleic acids of Cohen are capable of hybridizing to wildtype IKBKAP nucleic acids and thereby could detect nucleic acids

which contain a deletion of exon 20 by, for example, hybridization and detecting a change in size of the hybridized nucleic acid. Cohen does not teach packaging the primers and probes in a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, the Fodor (column 3) discloses the general concept of kits for performing nucleic acid hybridization methods and discloses that kits may include any of the reagents necessary for performing methods for detecting a target nucleic acid. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the IKBKAP nucleic acids of Cohen, including primers for amplifying IKBKAP and probes for detecting IKBKAP, in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art.

With respect to claims 73 and 74, Cohen does not teach further including oligonucleotides for detecting additional wildtype or mutant genes in a kit. However, Fodor (e.g., column 10) teaches arrays of probes which can be used to simultaneously detect distinct target nucleic acids, wherein the target nucleic acids may be either wildtype sequences or mutant sequences. The reference teaches that such arrays are useful for diagnosing a variety of diseases, including cystic fibrosis and teaches that the array may contain hundreds to thousands of probes (see column 19). Additionally, Fodor teaches kits containing arrays of nucleic acid probes (column 3). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included additional probes, such as probes to the cystic fibrosis gene, in

the kit containing probes and/or primers to the IKBKAP gene in order to have generated kits that could be used to simultaneously detect the presence of wildtype and/or mutant IKBKAP sequences and other diseases associated diseases.

RESPONSE TO ARGUMENTS:

In the response, Applicants traverse this rejection by stating that Cohen does not connect IKAP to FD and does not disclose the identity of mutations in the FD gene. This argument has been fully considered but is not persuasive. The claims are not limited to nucleic acids consisting of the FD1 or FD2 mutation. Rather, the claims are drawn broadly to encompass nucleic acid primers which amplify a region containing the FD1 or FD2 mutation. It is a property of the primers of Cohen that they can amplify this region of the FD gene.

16. Claims 55-57, 60 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slaugenhaupt (American Journal of Human Genetics (March 2001) 68: 598-605; cited in the IDS) in view of Cohen.

Slaugenhaupt (page 600) discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). Slaugenhaupt further teaches mutations in the IKBKAP wherein the first mutation is a G to C transversion at nucleotide 2397 in exon 19, resulting in an arginine to proline missense mutation at amino acid position 696 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 602). The reference also teaches amplification products containing the 2 mutations wherein the amplification products are generated by amplifying IKBKAP

sequences using primers to exons 19 and 20/21 (page 599). Slaugenhaupt does not specifically teach vectors and host cells comprising the IKBKAP cDNA or methods for producing IKBKAP wildtype or mutant proteins using host cells transformed with vectors containing IKBKAP cDNAs.

However, Cohen teaches an isolated nucleic acid encoding for IKBKAP (referred to therein as 'IKAP'; see SEQ ID NO: 1). Cohen (e.g., column 3) further teaches vectors and host cells comprising the IKBKAP cDNA. The reference (column 3 and 4) teaches methods for synthesizing recombinant IKBKAP using host cells transformed with IKBKAP, wherein the host cells are preferably human or other mammalian cells. Cohen (column 7-8) teaches use of the recombinant protein to identify compounds that bind to IKBKAP, which can then potentially be used for diagnostic and therapeutic applications.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the cDNAs of Slaugenhaupt into vectors, to have transformed host cells with the recombinant vectors and to have used the resulting transformed host cells to synthesize IKBKAP proteins in order to have provided recombinant IKBKAP wildtype and mutant proteins that could be used to further study the properties of these proteins and could be used in assays to identify potential diagnostic and therapeutic agents which bind IKBKAP proteins.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Slaugenhaupt is not prior art to the claimed invention because Applicants are entitled to the filing date of January 6, 2001. However, for the reasons stated above, the claims are not limited to the subject matter that is

entitled to the priority date of January 6, 2001 and thereby Slaugenhaupt is prior art to the claimed invention. Further, it is noted that, with respect to claim 75, while the provisional application provides support for SEQ ID NO: 2 and the mutation at position 2,397 of SEQ ID NO: 2, the provisional application does not appear to disclose a nucleic acid consisting of nucleotides 311 to 4,309 of SEQ ID NO: 2. In the response, it is stated that support for claim 75 may be found at page 4 of the specification or page 2 of the provisional application. However, the cited pages do not disclose a nucleic acid that begins at nucleotide position 311 of SEQ ID NO: 2 and ends at nucleotide position 4,309 of SEQ ID NO: 2. Accordingly, Slaugenhaupt is also prior art to the subject matter of claim 75.

17. Claims 55-57 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gill et al (GenBank Accession No. AF153419, published 02 January 2001) in view of Cohen.

Gill discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). The cDNA of Gill includes nucleotide position 2397 and hybridizes with IKBKAP nucleic acids comprising the 2397 FD mutation. Gill does not specifically teach vectors and host cells comprising the IKBKAP.

However, Cohen teaches an isolated nucleic acid encoding for IKBKAP (referred to therein as 'IKAP'; see SEQ ID NO: 1). Cohen (e.g., column 3) further teaches vectors and host cells comprising the IKBKAP cDNA. The reference (column 3 and 4) teaches methods for synthesizing recombinant IKBKAP using host cells transformed

with IKBKAP, wherein the host cells are preferably human or other mammalian cells. Cohen (column 7-8) teaches use of the recombinant protein to identify compounds that bind to IKBKAP, which can then potentially be used for diagnostic and therapeutic applications.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the cDNAs of Gill into vectors, to have transformed host cells with the recombinant vectors and to have used the resulting transformed host cells to synthesize IKBKAP proteins in order to have provided recombinant IKBKAP wildtype and mutant proteins that could be used to further study the properties of these proteins and could be used in assays to identify potential diagnostic and therapeutic agents which bind IKBKAP proteins.

RESPONSE TO ARGUMENTS:

In the response, Applicants traverse this rejection by stating that the claimed nucleic acid molecules require the presence of the FD1 or FD2 mutation and that Gill does not teach these mutations. This argument has been fully considered but is not persuasive because Applicants are arguing limitations that are not recited in the claims. The claims are not limited to nucleic acids which require the presence of the FD1 or FD2 mutation.

18. Claims 55-57 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slaugenhaupt et al (GenBank Accession No. AF153419, published 28 February 2001; cited in the IDS) in view of Cohen.

Slaugenhaupt discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). In the comments section of the sequence, it is noted that a polymorphism is present at nucleotide position 2397. The cDNA of Slaugenhaupt includes nucleotide position 2397 and hybridizes with IKBKAP nucleic acids comprising the 2397 FD mutation. Slaugenhaupt does not specifically teach vectors and host cells comprising the IKBKAP cDNA.

However, Cohen teaches an isolated nucleic acid encoding for IKBKAP (referred to therein as 'IKAP'; see SEQ ID NO: 1). Cohen (e.g., column 3) further teaches vectors and host cells comprising the IKBKAP cDNA. The reference (column 3 and 4) teaches methods for synthesizing recombinant IKBKAP using host cells transformed with IKBKAP, wherein the host cells are preferably human or other mammalian cells. Cohen (column 7-8) teaches use of the recombinant protein to identify compounds that bind to IKBKAP, which can then potentially be used for diagnostic and therapeutic applications.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the cDNAs of Slaugenhaupt into vectors, to have transformed host cells with the recombinant vectors and to have used the resulting transformed host cells to synthesize IKBKAP proteins in order to have provided recombinant IKBKAP wildtype and mutant proteins that could be used to further study the properties of these proteins and could be used in assays to identify potential diagnostic and therapeutic agents which bind IKBKAP proteins.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Slaugenhaupt is not prior art to the claimed invention because Applicants are entitled to the filing date of January 6, 2001. However, for the reasons stated above, the claims are not limited to the subject matter that is entitled to the priority date of January 6, 2001 and thereby Slaugenhaupt is prior art to the claimed invention.

19. Claims 61, 62, 64, 66-71, 73 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin in view of Fodor (U.S. Patent NO. 5,968,740).

Rubin (page 1, column 2) discloses a cDNA encoding IKBKAP having GenBank Accession No. NM_003640. This cDNA is 4803 bp in length, whereas the IKBKAP cDNA of the present invention (Figure 7 and SEQ ID NO :2) is 5924bp in length. Rubin further teaches mutations in the IKBKAP wherein the first mutation is a G to C transversion at nucleotide 2390 in exon 19 of Accession No. NM_003640 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 1, column 2). The reference also teaches primers for amplifying exons 19-21 (page 1, column 2 and page 2, column 1) and PCR amplification products containing each of the above mutations. Accordingly, Rubin teaches oligonucleotides for detecting a mutation in FD, wherein the oligonucleotide hybridizes to a FD mutation or to a region flanking a FD mutation. With respect to claims 62 and 64, the specification does not define the term "consisting essentially of" as it relates to the length of a nucleic acid, and thereby this phrase has been interpreted to included lengths comprising 399 or 500 nucleotides and lengths less than 399 and 500 nucleotides. With respect to claims 66-68, the primers of Rubin are able to amplify a region that contains a G or T (i.e., position

33,741 or 34,201 of SEQ ID NO: 1 and position 2,397 of SEQ ID NO: 2). With respect to claim 69, the nucleic acid of Cohen comprises SEQ ID NO: 86 wherein "S" is a "G." With respect to claims 70 and 71, the nucleic acids of Rubin are capable of hybridizing to wildtype IKBKAP nucleic acids and thereby could detect nucleic acids which contain a deletion of exon 20 by, for example, hybridization and detecting a change in size of the hybridized nucleic acid. Rubin does not teach packaging the IKBKAP oligonucleotides in a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, the Fodor (column 3) discloses the general concept of kits for performing nucleic acid hybridization methods and discloses that kits may include any of the reagents necessary for performing methods for detecting a target nucleic acid. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the IKBKAP nucleic acids of IKBKAP, including primers for amplifying IKBKAP and probes for detecting IKBKAP, in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art.

With respect to claims 73 and 74, Rubin does not teach further including oligonucleotides for detecting additional wildtype or mutant genes in a kit. However, Fodor (e.g., column 10) teaches arrays of probes which can be used to simultaneously detect distinct target nucleic acids, wherein the target nucleic acids may be either wildtype sequences or mutant sequences. The reference teaches that such arrays are useful for diagnosing a variety of diseases, including cystic fibrosis and teaches that the

array may contain hundreds to thousands of probes (see column 19). Additionally, Fodor teaches kits containing arrays of nucleic acid probes (column 3). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included additional probes, such as probes to the cystic fibrosis gene, in the kit containing probes and/or primers to the IKBKAP gene in order to have generated kits that could be used to simultaneously detect the presence of wildtype and/or mutant IKBKAP sequences and other diseases associated diseases.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Slaugenhaupt is not prior art to the claimed invention because Applicants are entitled to the filing date of January 6, 2001. However, for the reasons stated above, the claims are not limited to the subject matter that is entitled to the priority date of January 6, 2001 and thereby Slaugenhaupt is prior art to the claimed invention.

20. Claims 61, 62, 64, 66-71, 73 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson in view of Fodor (U.S. Patent NO. 5,968,740).

Anderson (page 754) discloses a cDNA encoding human IKBKAP having GenBank Accession No. NM_003640. This cDNA is 4803 bp in length, whereas the IKBKAP cDNA of the present invention (Figure 7 and SEQ ID NO :2) is 5924bp in length. Anderson further teaches mutations in the IKBKAP wherein the first mutation is a G to C transversion at nucleotide 2390 in exon 19 of Accession No. NM_003640 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 754). The reference also teaches primers for amplifying exons 19-21 (Figures 1

and 4) and PCR amplification products containing each of the above mutations. Accordingly, Anderson teaches oligonucleotides for detecting a mutation in FD, wherein the oligonucleotide hybridizes to a FD mutation or to a region flanking a FD mutation. With respect to claims 62 and 64, the specification does not define the term "consisting essentially of" as it relates to the length of a nucleic acid, and thereby this phrase has been interpreted to included lengths comprising 399 or 500 nucleotides and lengths less than 399 and 500 nucleotides. With respect to claims 66-68, the primers of Cohen are able to amplify a region that contains a G or T (i.e., position 33,741 or 34,201 of SEQ ID NO: 1 and position 2,397 of SEQ ID NO: 2). With respect to claim 69, the nucleic acid of Anderson comprises SEQ ID NO: 86. With respect to claims 70 and 71, the nucleic acids of Anderson are capable of hybridizing to wildtype IKBKAP nucleic acids and thereby could detect nucleic acids which contain a deletion of exon 20 by, for example, hybridization and detecting a change in size of the hybridized nucleic acid.

Anderson does not teach packaging the IKBKAP oligonucleotides in a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, the Fodor (column 3) discloses the general concept of kits for performing nucleic acid hybridization methods and discloses that kits may include any of the reagents necessary for performing methods for detecting a target nucleic acid. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the IKBKAP nucleic acids of IKBKAP, including

primers for amplifying IKBKAP and probes for detecting IKBKAP, in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art.

With respect to claims 73 and 74, Anderson does not teach further including oligonucleotides for detecting additional wildtype or mutant genes in a kit. However, Fodor (e.g., column 10) teaches arrays of probes which can be used to simultaneously detect distinct target nucleic acids, wherein the target nucleic acids may be either wildtype sequences or mutant sequences. The reference teaches that such arrays are useful for diagnosing a variety of diseases, including cystic fibrosis and teaches that the array may contain hundreds to thousands of probes (see column 19). Additionally, Fodor teaches kits containing arrays of nucleic acid probes (column 3). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included additional probes, such as probes to the cystic fibrosis gene, in the kit containing probes and/or primers to the IKBKAP gene in order to have generated kits that could be used to simultaneously detect the presence of wildtype and/or mutant IKBKAP sequences and other diseases associated diseases.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Anderson is not prior art to the claimed invention because Applicants are entitled to the filing date of January 6, 2001. However, for the reasons stated above, the claims are not limited to the subject matter that is entitled to the priority date of January 6, 2001 and thereby Anderson is prior art to the claimed invention.

21. Claims 61, 62, 64, 66-71, 73 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slaugenhaupt (American Journal of Human Genetics (March 2001) 68: 598-605; cited in the IDS) in view of Fodor (U.S. Patent NO. 5,968,740).

Slaugenhaupt (page 600) discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). Slaugenhaupt further teaches mutations in the IKBKAP wherein the first mutation is a G to C transversion at nucleotide 2397 in exon 19, resulting in a arginine to proline missense mutation at amino acid position 696 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 602). The reference also teaches amplification products containing the 2 mutations wherein the amplification products are generated by amplifying IKBKAP sequences using primers to exons 19 and 20/21 (page 599). Accordingly, Slaugenhaupt teaches oligonucleotides for detecting a mutation in FD, wherein the oligonucleotide hybridizes to a FD mutation. With respect to claims 62 and 64, the specification does not define the term "consisting essentially of" as it relates to the length of a nucleic acid, and thereby this phrase has been interpreted to included lengths comprising 399 or 500 nucleotides and lengths less than 399 and 500 nucleotides. With respect to claims 66-68, the primers of Slaugenhaupt are able to amplify a region that contains a G or T (i.e., position 33,741 or 34,201 of SEQ ID NO: 1 and position 2,397 of SEQ ID NO: 2). With respect to claim 69, the nucleic acid of Cohen comprises SEQ ID NO: 86 wherein "S" is a "G." With respect to claims 70 and 71, the nucleic acids are capable of hybridizing to wildtype IKBKAP nucleic acids and thereby could detect nucleic acids which contain a

deletion of exon 20 by, for example, hybridization and detecting a change in size of the hybridized nucleic acid. Slaugenhaupt does not teach packaging the IKBKAP oligonucleotides in a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, the Fodor (column 3) discloses the general concept of kits for performing nucleic acid hybridization methods and discloses that kits may include any of the reagents necessary for performing methods for detecting a target nucleic acid. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the IKBKAP nucleic acids of IKBKAP, including primers for amplifying IKBKAP and probes for detecting IKBKAP, in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art.

With respect to claims 73 and 74, Slaugenhaupt does not teach further including oligonucleotides for detecting additional wildtype or mutant genes in a kit. However, Fodor (e.g., column 10) teaches arrays of probes which can be used to simultaneously detect distinct target nucleic acids, wherein the target nucleic acids may be either wildtype sequences or mutant sequences. The reference teaches that such arrays are useful for diagnosing a variety of diseases, including cystic fibrosis and teaches that the array may contain hundreds to thousands of probes (see column 19). Additionally, Fodor teaches kits containing arrays of nucleic acid probes (column 3). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included additional probes, such as probes to the cystic fibrosis gene, in

the kit containing probes and/or primers to the IKBKAP gene in order to have generated kits that could be used to simultaneously detect the presence of wildtype and/or mutant IKBKAP sequences and other diseases associated diseases.

RESPONSE TO ARGUMENTS:

In the response, Applicants state that Slaugenhaupt is not prior art to the claimed invention because Applicants are entitled to the filing date of January 6, 2001. However, for the reasons stated above, the claims are not limited to the subject matter that is entitled to the priority date of January 6, 2001 and thereby Slaugenhaupt is prior art to the claimed invention.

22. Claims 61, 62, 64, 66-71, 73 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gill in view of Cohen and further in view of Fodor (U.S. Patent NO. 5,968,740).

The teachings of Gill and Cohen are presented above. The combined references teach a IKBKAP cDNA of 5.9 Kb identical to the cDNA of present SEQ ID NO: 1. The combined references also teach detecting IKBKAP nucleic acids using oligonucleotide probes and primers. The combined references not teach packaging the IKBKAP oligonucleotides in a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, the Fodor (column 3) discloses the general concept of kits for performing nucleic acid hybridization methods and discloses that kits may include any of the reagents necessary for performing methods for detecting a target nucleic acid. Accordingly, it

would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the IKBKAP nucleic acids of IKBKAP, including primers for amplifying IKBKAP and probes for detecting IKBKAP, in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art.

With respect to claims 73 and 74, Gill and Cohen do not teach further including oligonucleotides for detecting additional wildtype or mutant genes in a kit. However, Fodor (e.g., column 10) teaches arrays of probes which can be used to simultaneously detect distinct target nucleic acids, wherein the target nucleic acids may be either wildtype sequences or mutant sequences. The reference teaches that such arrays are useful for diagnosing a variety of diseases, including cystic fibrosis and teaches that the array may contain hundreds to thousands of probes (see column 19). Additionally, Fodor teaches kits containing arrays of nucleic acid probes (column 3). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included additional probes, such as probes to the cystic fibrosis gene, in the kit containing probes and/or primers to the IKBKAP gene in order to have generated kits that could be used to simultaneously detect the presence of wildtype and/or mutant IKBKAP sequences and other diseases associated diseases.

RESPONSE TO ARGUMENTS:

In the response, Applicants traverse this rejection by stating that Gill does not connect IKAP to FD and does not disclose the identity of mutations in the FD gene. This argument has been fully considered but is not persuasive. The claims are not limited to nucleic acids consisting of the FD1 or FD2 mutation. Rather, the claims are drawn

broadly to encompass nucleic acid primers which amplify a region containing the FD1 or FD2 mutation. It is a property of the oligonucleotides disclosed by the combined art of Gill and Cohen that these oligonucleotides can amplify regions of the FD gene containing the FD1 and FD2 mutations.

23. Claims 61, 62, 64, 66-71, 73 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slaugenhaupt et al (GenBank Accession No. AF153419, published 28 February 2001; cited in the IDS) in view of Cohen and further in view of Fodor (U.S. Patent NO. 5,968,740).

The teachings of Slaugenhaupt and Cohen are presented above. The combined references teach a IKBKAP cDNA of 5.9 Kb identical to the cDNA of present SEQ ID NO: 1. The combined references also teach detecting IKBKAP nucleic acids using oligonucleotide probes and primers. With respect to claims 62 and 64, the specification does not define the term "consisting essentially of" as it relates to the length of a nucleic acid, and thereby this phrase has been interpreted to included lengths comprising 399 or 500 nucleotides and lengths less than 399 and 500 nucleotides. With respect to claims 66-68, the primers of Slaugenhaupt are able to amplify a region that contains a G or T (i.e., position 33,741 or 34,201 of SEQ ID NO: 1 and position 2,397 of SEQ ID NO: 2). With respect to claim 69, the nucleic acids comprises SEQ ID NO: 86. With respect to claims 70 and 71, the nucleic acids are capable of hybridizing to wildtype IKBKAP nucleic acids and thereby could detect nucleic acids which contain a deletion of exon 20 by, for example, hybridization and detecting a change in size of the hybridized nucleic

acid. The combined references not teach packaging the IKBKAP oligonucleotides in a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, the Fodor (column 3) discloses the general concept of kits for performing nucleic acid hybridization methods and discloses that kits may include any of the reagents necessary for performing methods for detecting a target nucleic acid. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the IKBKAP nucleic acids of IKBKAP, including primers for amplifying IKBKAP and probes for detecting IKBKAP, in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art.

With respect to claims 73 and 74, Slaugenhaupt and Cohen do not teach further including oligonucleotides for detecting additional wildtype or mutant genes in a kit. However, Fodor (e.g., column 10) teaches arrays of probes which can be used to simultaneously detect distinct target nucleic acids, wherein the target nucleic acids may be either wildtype sequences or mutant sequences. The reference teaches that such arrays are useful for diagnosing a variety of diseases, including cystic fibrosis and teaches that the array may contain hundreds to thousands of probes (see column 19). Additionally, Fodor teaches kits containing arrays of nucleic acid probes (column 3). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included additional probes, such as probes to the cystic fibrosis gene, in the kit containing probes and/or primers to the IKBKAP gene in order to

have generated kits that could be used to simultaneously detect the presence of wildtype and/or mutant IKBKAP sequences and other diseases associated diseases.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

24. Claims 58 and 59 rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen in view of Ghosh (U.S. Patent NO. 5,597,898).

The teachings of Cohen are presented above. In particular, Cohen (columns 3 and 5) teaches expression of IKAP nucleic acids in mammalian cells. Cohen does not teach expression of IKAP nucleic acids in yeast or E. coli host cells.

However, Ghosh (see, e.g., paragraphs 21 and 23) teaches alternative host cells for expressing mammalian nucleic acids including yeast and E. coli host cells.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the recombinant vectors of Cohen containing IKAP nucleic acids into yeast or E. coli host cells, in place of mammalian host cells, in order to have provided an equally effective means for expressing IKAP nucleic acids and of providing host cells that were readily available and convenient to use for cloning and culturing purposes.

25. Claims 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slaugenhaupt (American Journal of Human Genetics (March 2001) 68: 598-605; cited in the IDS) in view of Cohen and further in view of Ghosh (U.S. Patent NO. 5,597,898).

The teachings of Slaugenhaupt and Cohen are presented above. In particular, the combined references teach expression of IKAP nucleic acids in mammalian cells.

The combined references do not teach expression of IKAP nucleic acids in yeast or E. coli host cells.

However, Ghosh (see, e.g., paragraphs 21 and 23) teaches alternative host cells for expressing mammalian nucleic acids including yeast and E. coli host cells.
It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the recombinant vectors containing IKAP nucleic acids into yeast or E. coli host cells, in place of mammalian host cells, in order to have provided an equally effective means for expressing IKAP nucleic acids and of providing host cells that were readily available and convenient to use for cloning and culturing purposes.

26. Claims 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gill et al in view of Cohen and further in view of Ghosh.

The teachings of Gill and Cohen are presented above. In particular, the combined references teach expression of IKAP nucleic acids in mammalian cells. The combined references do not teach expression of IKAP nucleic acids in yeast or E. coli host cells.

However, Ghosh (see, e.g., paragraphs 21 and 23) teaches alternative host cells for expressing mammalian nucleic acids including yeast and E. coli host cells.
It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the recombinant vectors containing IKAP nucleic acids into yeast or E. coli host cells, in place of mammalian host cells, in order to have provided an equally effective means for expressing IKAP nucleic acids and of providing host cells that were readily available and convenient to use for cloning and culturing purposes.

27. Claims 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slaugenhaupt et al (GenBank Accession No. AF153419, published 28 February 2001; cited in the IDS) in view of Cohen and further in view of Ghosh.

The teachings of Slaugenhaupt and Cohen are presented above. In particular, the combined references teach expression of IKAP nucleic acids in mammalian cells. The combined references do not teach expression of IKAP nucleic acids in yeast or E. coli host cells.

However, Ghosh (see, e.g., paragraphs 21 and 23) teaches alternative host cells for expressing mammalian nucleic acids including yeast and E. coli host cells.
It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the recombinant vectors containing IKAP nucleic acids into yeast or E. coli host cells, in place of mammalian host cells, in order to have provided an equally effective means for expressing IKAP nucleic acids and of providing host cells that were readily available and convenient to use for cloning and culturing purposes.
28. Claims 55-57, 60 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin in view of Cohen.

Rubin (page 1, column 2) discloses a cDNA encoding IKBKAP having GenBank Accession No. NM_003640. This cDNA is 4803 bp in length, whereas the IKBKAP cDNA of the present invention (Figure 7 and SEQ ID NO :2) is 5924bp in length. Rubin further teaches mutations in the IKBKAP wherein the first mutation is a G to C transversion at nucleotide 2390 in exon 19 of Accession No. NM_003640 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6

(page 1, column 2). Gill discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). The cDNA of Gill includes nucleotide position 2397 and hybridizes with IKBKAP nucleic acids comprising the 2397 FD mutation. Rubin does not specifically teach vectors and host cells comprising the IKAP cDNA or methods for producing mutant IKAP proteins using host cells transformed with vectors containing IKAP cDNAs.

However, Cohen teaches an isolated nucleic acid encoding for IKBKAP (referred to therein as 'IKAP'; see SEQ ID NO: 1). Cohen (e.g., column 3) further teaches vectors and host cells comprising the IKBKAP cDNA. The reference (column 3 and 4) teaches methods for synthesizing recombinant IKBKAP using host cells transformed with IKBKAP, wherein the host cells are preferably human or other mammalian cells. Cohen (column 7-8) teaches use of the recombinant protein to identify compounds that bind to IKBKAP, which can then potentially be used for diagnostic and therapeutic applications.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the cDNAs of Rubin into vectors, to have transformed host cells with the recombinant vectors and to have used the resulting transformed host cells to synthesize IKBKAP proteins in order to have provided recombinant IKBKAP wildtype and mutant proteins that could be used to further study the properties of these proteins and could be used in assays to identify potential diagnostic and therapeutic agents which bind IKBKAP proteins.

29. Claims 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin in view of Cohen and further in view of Ghosh.

The teachings of Rubin and Cohen are presented above. In particular, the combined references teach expression of IKAP nucleic acids in mammalian cells. The combined references do not teach expression of IKAP nucleic acids in yeast or E. coli host cells.

However, Ghosh (see, e.g., paragraphs 21 and 23) teaches alternative host cells for expressing mammalian nucleic acids including yeast and E. coli host cells.
It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the recombinant vectors containing IKAP nucleic acids into yeast or E. coli host cells, in place of mammalian host cells, in order to have provided an equally effective means for expressing IKAP nucleic acids and of providing host cells that were readily available and convenient to use for cloning and culturing purposes.
30. Claims 55-57, 60 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson in view of Cohen.

Anderson (page 754) discloses a cDNA encoding human IKBKAP having GenBank Accession No. NM_003640. This cDNA is 4803 bp in length, whereas the IKBKAP cDNA of the present invention (Figure 7 and SEQ ID NO :2) is 5924bp in length. Anderson further teaches mutations in the IKBKAP wherein the first mutation is a G to C transversion at nucleotide 2390 in exon 19 of Accession No. NM_003640 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 754). Anderson does not specifically teach vectors and host cells comprising the

IKAP cDNA or methods for producing mutant IKAP proteins using host cells transformed with vectors containing IKAP cDNAs.

However, Cohen teaches an isolated nucleic acid encoding for IKBKAP (referred to therein as 'IKAP'; see SEQ ID NO: 1). Cohen (e.g., column 3) further teaches vectors and host cells comprising the IKBKAP cDNA. The reference (column 3 and 4) teaches methods for synthesizing recombinant IKBKAP using host cells transformed with IKBKAP, wherein the host cells are preferably human or other mammalian cells. Cohen (column 7-8) teaches use of the recombinant protein to identify compounds that bind to IKBKAP, which can then potentially be used for diagnostic and therapeutic applications.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the cDNAs of Anderson into vectors, to have transformed host cells with the recombinant vectors and to have used the resulting transformed host cells to synthesize IKBKAP proteins in order to have provided recombinant IKBKAP wildtype and mutant proteins that could be used to further study the properties of these proteins and could be used in assays to identify potential diagnostic and therapeutic agents which bind IKBKAP proteins.

31. Claims 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson in view of Cohen and further in view of Ghosh.

The teachings of Anderson and Cohen are presented above. In particular, the combined references teach expression of IKAP nucleic acids in mammalian cells. The

combined references do not teach expression of IKAP nucleic acids in yeast or E. coli host cells.

However, Ghosh (see, e.g., paragraphs 21 and 23) teaches alternative host cells for expressing mammalian nucleic acids including yeast and E. coli host cells.
It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned the recombinant vectors containing IKAP nucleic acids into yeast or E. coli host cells, in place of mammalian host cells, in order to have provided an equally effective means for expressing IKAP nucleic acids and of providing host cells that were readily available and convenient to use for cloning and culturing purposes.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers
November 21, 2005

CARLA J. MYERS
PRIMARY EXAMINER

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DE   Human differential transcription-associated cDNA SEQ ID 276.
XX
KW   Differential transcription; human; rat; tumour cell; cytostatic;
KW   Ras modulator; Class II tumour suppressor gene; gene therapy; ss.
XX
OS   Homo sapiens.
XX
PN   WO200157058-A2.
XX
PD   09-AUG-2001.
XX
PF   31-JAN-2001; 2001WO-EP001003.
XX
PR   31-JAN-2000; 2000DE-01004102.
XX
PA   (META-) METAGEN GES GENOMFORSCHUNG MBH.
XX
PI   Rosenthal A,  Hinzmann B,  Schaefer R,  Zuber J,  Tchernitsa O;
PI   Grips M,  Hellriegel M,  Schmitz A,  Sers C;
XX
DR   WPI; 2001-483415/52.
XX
PT   Nucleic acids differentially expressed between tumor and normal cells,
PT   useful for diagnosis or therapy of tumors and for screening active
PT   agents.
XX
PS   Disclosure; Page 430-431; 579pp; German.
XX
CC   This invention describes a nucleic acid (I) with differential expression
CC   between tumour and normal cells and which has cytostatic activity. (I)
CC   work as modulators of Ras activity by inducing expression of tumour
CC   suppressor genes. (I), and polypeptides encoded by them, are useful as
CC   targets for diagnosis or therapy and in screening to determine the
CC   effects of an active compound (potential pharmaceutical) on a cell line,
CC   particularly for diagnosis and treatment of tumors, especially by
CC   modulating expression of (I) (by gene therapy, antisense RNA or ribozyme
CC   methods) or by modulating the amount and/or location of (I)-encoded
CC   polypeptides (by administration of the polypeptide or its activator,
CC   antibody (optionally as a conjugate) or inhibitor). The method allows
CC   identification of many Class II tumour suppressor genes (i.e. genes that
CC   are not primary targets for tumour-initiating mutations). AAH81492-
CC   AAH82376 represent the human and rat derived nucleic acid fragments
CC   described in the method of the invention
XX
SQ   Sequence 4803 BP; 1325 A; 1015 C; 1192 G; 1271 T; 0 U; 0 Other;

  Query Match             97.3%;  Score 14.6;  DB 5;  Length 4803;
  Best Local Similarity   93.3%;  Pred. No. 1.3e+02;
  Matches   14;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GGTTCACSGATTGTC 15
              |||||||:|||||||
Db       2383 GGTTCACGGATTGTC 2397


RESULT 9
AAL44190
ID   AAL44190 standard; DNA; 4803 BP.
XX
AC   AAL44190;
XX
DT   24-OCT-2002  (first entry)
XX
DE   Human I-kappa beta associated protein (IKAP) gene sequence.
XX
KW   Human; gene; ds; single nucleotide polymorphism; SNP; bronchial asthma;
KW   I-kappa beta associated protein; IKAP; infant bronchial asthma.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             304. .4302
FT                   /*tag=  a
FT                   /product= "Human I-kappa beta associated protein (IKAP)"
XX
PN   WO200259305-A1.
XX
PD   01-AUG-2002.
XX
PF   25-JAN-2002; 2002WO-JP000540.
XX
PR   25-JAN-2001; 2001JP-00017076.
XX
PA   (SAKA ) OTSUKA PHARM CO LTD.
XX
PI   Nakamura Y,  Tamari M;
XX
DR   WPI; 2002-557950/59.
DR   P-PSDB; AAO15505.
XX
PT   Detection of specific single nucleotide polymorphisms in human I-kappa
PT   beta associated protein for analysis of etiology of bronchial asthma.
XX
PS   Claim 7; Page 45-48; 60pp; Japanese.
XX
CC   The invention comprises a method for detecting single nucleotide
CC   polymorphisms (SNPs) in genes associated with human bronchial asthma. The
CC   method specifically refers to detecting polymorphisms in the gene
CC   encoding human I-kappa beta associated protein (IKAP). The invention also
CC   comprises primers and probes for use in the method of the invention. The
CC   method of the invention is useful for analysis of the etiology of
CC   bronchial asthma (especially infant bronchial asthma). The present DNA
CC   sequence encodes the human I-kappa beta associated protein
XX
SQ   Sequence 4803 BP; 1324 A; 1014 C; 1193 G; 1272 T; 0 U; 0 Other;

  Query Match             97.3%;  Score 14.6;  DB 6;  Length 4803;
  Best Local Similarity   93.3%;  Pred. No. 1.3e+02;
  Matches   14;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GGTTCACSGATTGTC 15
              |||||||:|||||||
Db       2383 GGTTCACGGATTGTC 2397


RESULT 10
ABQ80570
ID   ABQ80570 standard; cDNA; 5924 BP.
XX
AC   ABQ80570;
XX
DT   08-NOV-2002  (first entry)
XX
DE   Mutant human IKBKAP coding sequence.
XX
KW   Human; IKBKAP; Familial Dysautonomia; FD; Riley-Day syndrome; gene; ss;
KW   Hereditary Sensory and Autonomic Neuropathy Type III; carrier screening;
KW   mutation.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   CDS             311. .4309
FT                   /*tag=  a
FT                   /product= "IKBKAP #2"
FT                   /transl_except= (pos:1220. .1222,aa:Arg)
FT                   /transl_except= (pos:1244. .1246,aa:Lys)
FT                   /transl_except= (pos:2570. .2572,aa:Pro)
FT   mutation        replace(2397,G)
FT                   /*tag=  b
XX
PN   WO200259381-A2.
XX
PD   01-AUG-2002.
XX
```

PF 07-JAN-2002; 2002WO-US000473.
XX
PR 06-JAN-2001; 2001US-0260080P.
XX
PA (GEHO) GEN HOSPITAL CORP.
XX
PI Slaugenhaupt S, Gusella JF;
XX
DR WPI; 2002-674806/72.
DR P-PSDB; ABB98493.
XX
PT New IKBKAP genes with mutations, useful for identifying a subject with
PT familial dysautonomia (FD), or for rapid carrier screening in the
PT Ashkenazi Jewish population, e.g. screening presymptomatic homozygotes or
PT prenatal diagnosis.
XX
PS Claim 1; Page; 109pp; English.
XX
CC The present invention relates to methods and compositions useful for
CC detecting mutations which cause Familial Dysautonomia (FD, Riley-Day
CC syndrome, Hereditary Sensory and Autonomic Neuropathy Type III) [OMIM
CC 223900]. It was found that mutations in the IKBKAP gene (see ABQ80565)
CC are associated with FD. The mutation associated with the major haplotype
CC of FD, FD1 mutation, is a base pair (bp) mutation, where the thymine
CC nucleotide located at bp 6 of intron 20 in the IKBKAP gene is replaced
CC with a cytosine. This results in skipping of exon 20 in the mRNA from FD
CC patients, although they continue to express varying levels of wild-type
CC message in a tissue-specific manner. The mutation associated with the
CC minor haplotype, FD2 mutation, is a bp mutation, where the guanine
CC nucleotide at bp 2397 (bp 73 of exon 19) is replaced with a cytosine.
CC This bp mutation causes an arginine to proline missense mutation (R696P)
CC in the IKBKAP protein, which is predicted to disrupt a potential
CC phosphorylation site. The IKBKAP nucleic acid sequences are useful for
CC identifying a subject with FD and for rapid carrier screening. The IKBKAP
CC gene maps to chromosome 9q31. The present sequence is a mutant IKBKAP
CC coding sequence. Note: the present sequence was not shown in the
CC specification, but was derived from the human wild-type IKBKAP sequence
CC given in Fig 7
XX
SQ Sequence 5924 BP; 1662 A; 1225 C; 1392 G; 1645 T; 0 U; 0 Other;

Query Match 97.3%; Score 14.6; DB 6; Length 5924;
Best Local Similarity 93.3%; Pred. No. 1.4e+02;
Matches 14; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 GGTTCACSGATTGTC 15
||||||:|||||||
Db 2390 GGTTCACCGATTGTC 2404

RESULT 11
ABQ80569
ID ABQ80569 standard; cDNA; 5924 BP.
XX
AC ABQ80569;
XX
DT 08-NOV-2002 (first entry)
XX
DE Human IKBKAP wild-type coding sequence.
XX
KW Human; IKBKAP; Familial Dysautonomia; FD; Riley-Day syndrome; gene; ss;
KW Hereditary Sensory and Autonomic Neuropathy Type III; carrier screening;
KW chromosome 9q31.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT CDS 311. .4309
FT /*tag= a
FT /product= "IKBKAP #1"
FT /transl_except= (pos:1220. .1222,aa:Arg)
FT /transl_except= (pos:1244. .1246,aa:Lys)
FT /transl_except= (pos:2570. .2572,aa:Pro)

XX
PN WO200259381-A2.
XX
PD 01-AUG-2002.
XX
PF 07-JAN-2002; 2002WO-US000473.
XX
PR 06-JAN-2001; 2001US-0260080P.
XX
PA (GEHO) GEN HOSPITAL CORP.
XX
PI Slaugenhaupt S, Gusella JF;
XX
DR WPI; 2002-674806/72.
DR P-PSDB; ABB98492.
XX
PT New IKBKAP genes with mutations, useful for identifying a subject with
PT familial dysautonomia (FD), or for rapid carrier screening in the
PT Ashkenazi Jewish population, e.g. screening presymptomatic homozygotes or
PT prenatal diagnosis.
XX
PS Claim 1; Fig 7; 109pp; English.
XX
CC The present invention relates to methods and compositions useful for
CC detecting mutations which cause Familial Dysautonomia (FD, Riley-Day
CC syndrome, Hereditary Sensory and Autonomic Neuropathy Type III) [OMIM
CC 223900]. It was found that mutations in the IKBKAP gene (see ABQ80565)
CC are associated with FD. The mutation associated with the major haplotype
CC of FD, FD1 mutation, is a base pair (bp) mutation, where the thymine
CC nucleotide located at bp 6 of intron 20 in the IKBKAP gene is replaced
CC with a cytosine. This results in skipping of exon 20 in the mRNA from FD
CC patients, although they continue to express varying levels of wild-type
CC message in a tissue-specific manner. The mutation associated with the
CC minor haplotype, FD2 mutation, is a bp mutation, where the guanine
CC nucleotide at bp 2397 (bp 73 of exon 19) is replaced with a cytosine.
CC This bp mutation causes an arginine to proline missense mutation (R696P)
CC in the IKBKAP protein, which is predicted to disrupt a potential
CC phosphorylation site. The IKBKAP nucleic acid sequences are useful for
CC identifying a subject with FD and for rapid carrier screening. The IKBKAP
CC gene maps to chromosome 9q31. The present sequence is the IKBKAP coding
CC sequence
XX
SQ Sequence 5924 BP; 1662 A; 1224 C; 1393 G; 1645 T; 0 U; 0 Other;

Query Match 97.3%; Score 14.6; DB 6; Length 5924;
Best Local Similarity 93.3%; Pred. No. 1.4e+02;
Matches 14; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 GGTTCACSGATTGTC 15
||||||:|||||||
Db 2390 GGTTCACGGATTGTC 2404

RESULT 12
ACD13384
ID ACD13384 standard; cDNA; 5924 BP.
XX
AC ACD13384;
XX
DT 13-AUG-2003 (first entry)
XX
DE Human DNA encoding a p53 modifier, SEQ ID 55.
XX
KW Human; ss; gene; p53 modifier; cytostatic; cancer; cytostatic;
KW antiangiogenic; antiapoptotic; p53 pathway; breast cancer; colon cancer;
KW kidney cancer; lung cancer; ovarian cancer; angiogenesis; cell cycle;
KW apoptotic disorder; cell proliferation disorder.
XX
OS Homo sapiens.
XX
PN WO200299122-A1.
XX
PD 12-DEC-2002.

XX
PF 03-JUN-2002; 2002WO-US017382.
XX
PR 05-JUN-2001; 2001US-0296076P.
PR 10-OCT-2001; 2001US-0328605P.
PR 15-FEB-2002; 2002US-0357253P.
XX
PA (EXEL-) EXELIXIS INC.
XX
PI Friedman L, Plowman GD, Belvin M, Francis-Lang H, Li D, Funke RP;
XX
DR WPI; 2003-156859/15.
DR P-PSDB; ABO07210.
XX
PT Identifying modulators of the p53 pathway for use in treating apoptotic
PT or cell proliferation disorders, comprises screening for agents that
PT modulate activity of a human ortholog of genes that modify the p53
PT pathway in Drosophila.
XX
PS Example 2; Page 302-304; 678pp; English.
XX
CC The invention relates to identifying (M1) a candidate p53 pathway
CC modulating agent, by contacting an assay system comprising a purified HM
CC polypeptide (human orthologue of genes that modify the p53 pathway in
CC Drosophila) or nucleic acid with a test agent under conditions, where but
CC for the presence of the test agent, the system provides a reference
CC activity, and detecting a test agent-biased activity of the assay system.
CC Also included are modulating (M2) a p53 pathway of a cell (comprising
CC contacting a cell defective in p53 function with a candidate modulator
CC that specifically binds to a HM polypeptide comprising an HM amino acid
CC sequence, where p53 function is restored), modulating (M3) a p53 pathway
CC in a mammalian cell (comprising contacting the cell with an agent that
CC specifically binds an HM polypeptide or nucleic acid) and diagnosing (M4)
CC a disease in a patient (comprising: (a) obtaining a biological sample
CC from the patient; (b) contacting the sample with a probe for HM
CC expression; (c) comparing the results with a control; and (d) determining
CC whether the comparison indicates a likelihood disease). (M1) is useful
CC for identifying modulators of the p53 pathway. A probe for HM expression
CC is useful for diagnosing breast, colon, kidney, lung and ovarian cancer,
CC in a patient, where the cancer has greater than 25 % expression level.
CC Modulators identified by (M1) are useful in a variety of diagnostic and
CC therapeutic applications, where disease or disorder prognosis is related
CC to defects in the p53 pathway, such as, angiogenesis, apoptotic or cell
CC proliferation disorders (e.g. cancer). Another two new methods (M2 and
CC M3) are useful for modulating the p53 pathway of a cell, thus restoring
CC the p53 function of the cell, so that the cell undergoes normal
CC proliferation or progression through the cell cycle. (M2) and (M3) are
CC also useful for treating defects in the p53 pathway such as angiogenic,
CC apoptotic or cell proliferation disorders. The present sequence is an HM
CC nucleic acid encoding a p53 pathway modifying protein
XX
SQ Sequence 5924 BP; 1662 A; 1224 C; 1393 G; 1645 T; 0 U; 0 Other;

Query Match 97.3%; Score 14.6; DB 8; Length 5924;
Best Local Similarity 93.3%; Pred. No. 1.4e+02;
Matches 14; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 GGTTCACSGATTGTC 15
||||||:|||||||
Db 2390 GGTTCACGGATTGTC 2404

RESULT 13
ABQ80567
ID ABQ80567 standard; DNA; 66479 BP.
XX
AC ABQ80567;
XX
DT 08-NOV-2002 (first entry)
XX
DE Mutant human IKBKAP gene #2.
XX
KW Human; IKBKAP; Familial Dysautonomia; FD; Riley-Day syndrome;
KW Hereditary Sensory and Autonomic Neuropathy Type III; carrier screening;
KW FD2; mutation; gene; chromosome 9q31; ds.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT mutation replace(33714,G)
FT /*tag= a
XX
PN WO200259381-A2.
XX
PD 01-AUG-2002.
XX
PF 07-JAN-2002; 2002WO-US000473.
XX
PR 06-JAN-2001; 2001US-0260080P.
XX
PA (GEHO) GEN HOSPITAL CORP.
XX
PI Slaugenhaupt S, Gusella JF;
XX
DR WPI; 2002-674806/72.
XX
PT New IKBKAP genes with mutations, useful for identifying a subject with
PT familial dysautonomia (FD), or for rapid carrier screening in the
PT Ashkenazi Jewish population, e.g. screening presymptomatic homozygotes or
PT prenatal diagnosis.
XX
PS Claim 1; Page; 109pp; English.
XX
CC The present invention relates to methods and compositions useful for
CC detecting mutations which cause Familial Dysautonomia (FD, Riley-Day
CC syndrome, Hereditary Sensory and Autonomic Neuropathy Type III) [OMIM
CC 223900]. It was found that mutations in the IKBKAP gene (see ABQ80565)
CC are associated with FD. The mutation associated with the major haplotype
CC of FD, FD1 mutation, is a base pair (bp) mutation, where the thymine
CC nucleotide located at bp 6 of intron 20 in the IKBKAP gene is replaced
CC with a cytosine. This results in skipping of exon 20 in the mRNA from FD
CC patients, although they continue to express varying levels of wild-type
CC message in a tissue-specific manner. The mutation associated with the
CC minor haplotype, FD2 mutation, is a bp mutation, where the guanine
CC nucleotide at bp 2397 (bp 73 of exon 19) is replaced with a cytosine.
CC This bp mutation causes an arginine to proline missense mutation (R696P)
CC in the IKBKAP protein, which is predicted to disrupt a potential
CC phosphorylation site. The IKBKAP nucleic acid sequences are useful for
CC identifying a subject with FD and for rapid carrier screening. The IKBKAP
CC gene contains 37 exons and maps to chromosome 9q31. Note: the present
CC sequence was not shown in the specification, but was derived from the
CC human wild-type IKBKAP sequence given in Fig 6
XX
SQ Sequence 66479 BP; 18271 A; 12399 C; 14128 G; 21681 T; 0 U; 0 Other;

Query Match 97.3%; Score 14.6; DB 6; Length 66479;
Best Local Similarity 93.3%; Pred. No. 1.7e+02;
Matches 14; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 GGTTCACSGATTGTC 15
||||||:|||||||
Db 33707 GGTTCACCGATTGTC 33721

RESULT 14
ABQ80566
ID ABQ80566 standard; DNA; 66479 BP.
XX
AC ABQ80566;
XX
DT 08-NOV-2002 (first entry)
XX
DE Mutant human IKBKAP gene #1.
XX
KW Human; IKBKAP; Familial Dysautonomia; FD; Riley-Day syndrome;

```
KW   Hereditary Sensory and Autonomic Neuropathy Type III; carrier screening;
KW   FD1; mutation; gene; chromosome 9q31; ds.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   mutation        replace(34201,T)
FT                   /*tag=  a
XX
PN   WO200259381-A2.
XX
PD   01-AUG-2002.
XX
PF   07-JAN-2002; 2002WO-US000473.
XX
PR   06-JAN-2001; 2001US-0260080P.
XX
PA   (GEHO ) GEN HOSPITAL CORP.
XX
PI   Slaugenhaupt S,  Gusella JF;
XX
DR   WPI; 2002-674806/72.
XX
PT   New IKBKAP genes with mutations, useful for identifying a subject with
PT   familial dysautonomia (FD), or for rapid carrier screening in the
PT   Ashkenazi Jewish population, e.g. screening presymptomatic homozygotes or
PT   prenatal diagnosis.
XX
PS   Claim 1; Page; 109pp; English.
XX
CC   The present invention relates to methods and compositions useful for
CC   detecting mutations which cause Familial Dysautonomia (FD, Riley-Day
CC   syndrome, Hereditary Sensory and Autonomic Neuropathy Type III) [OMIM
CC   223900]. It was found that mutations in the IKBKAP gene (see ABQ80565)
CC   are associated with FD. The mutation associated with the major haplotype
CC   of FD, FD1 mutation, is a base pair (bp) mutation, where the thymine
CC   nucleotide located at bp 6 of intron 20 in the IKBKAP gene is replaced
CC   with a cytosine. This results in skipping of exon 20 in the mRNA from FD
CC   patients, although they continue to express varying levels of wild-type
CC   message in a tissue-specific manner. The mutation associated with the
CC   minor haplotype, FD2 mutation, is a bp mutation, where the guanine
CC   nucleotide at bp 2397 (bp 73 of exon 19) is replaced with a cytosine.
CC   This bp mutation causes an arginine to proline missense mutation (R696P)
CC   in the IKBKAP protein, which is predicted to disrupt a potential
CC   phosphorylation site. The IKBKAP nucleic acid sequences are useful for
CC   identifying a subject with FD and for rapid carrier screening. The IKBKAP
CC   gene contains 37 exons and maps to chromosome 9q31. Note: the present
CC   sequence was not shown in the specification, but was derived from the
CC   human wild-type IKBKAP sequence given in Fig 6
XX
SQ   Sequence 66479 BP; 18271 A; 12399 C; 14129 G; 21680 T; 0 U; 0 Other;

  Query Match             97.3%;  Score 14.6;  DB 6;  Length 66479;
  Best Local Similarity   93.3%;  Pred. No. 1.7e+02;
  Matches   14;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GGTTCACSGATTGTC 15
              |||||||:|||||||
Db      33707 GGTTCACGGATTGTC 33721


RESULT 15
ABQ80568
ID   ABQ80568 standard; DNA; 66479 BP.
XX
AC   ABQ80568;
XX
DT   08-NOV-2002  (first entry)
XX
DE   Mutant human IKBKAP gene #3.
XX
KW   Human; IKBKAP; Familial Dysautonomia; FD; Riley-Day syndrome;
```

```
KW   Hereditary Sensory and Autonomic Neuropathy Type III; carrier screening;
KW   FD1; FD2; mutation; gene; chromosome 9q31; ds.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   mutation        replace(33714,G)
FT                   /*tag=  a
FT   mutation        replace(34201,T)
FT                   /*tag=  b
XX
PN   WO200259381-A2.
XX
PD   01-AUG-2002.
XX
PF   07-JAN-2002; 2002WO-US000473.
XX
PR   06-JAN-2001; 2001US-0260080P.
XX
PA   (GEHO ) GEN HOSPITAL CORP.
XX
PI   Slaugenhaupt S,  Gusella JF;
XX
DR   WPI; 2002-674806/72.
XX
PT   New IKBKAP genes with mutations, useful for identifying a subject with
PT   familial dysautonomia (FD), or for rapid carrier screening in the
PT   Ashkenazi Jewish population, e.g. screening presymptomatic homozygotes or
PT   prenatal diagnosis.
XX
PS   Claim 1; Page; 109pp; English.
XX
CC   The present invention relates to methods and compositions useful for
CC   detecting mutations which cause Familial Dysautonomia (FD, Riley-Day
CC   syndrome, Hereditary Sensory and Autonomic Neuropathy Type III) [OMIM
CC   223900]. It was found that mutations in the IKBKAP gene (see ABQ80565)
CC   are associated with FD. The mutation associated with the major haplotype
CC   of FD, FD1 mutation, is a base pair (bp) mutation, where the thymine
CC   nucleotide located at bp 6 of intron 20 in the IKBKAP gene is replaced
CC   with a cytosine. This results in skipping of exon 20 in the mRNA from FD
CC   patients, although they continue to express varying levels of wild-type
CC   message in a tissue-specific manner. The mutation associated with the
CC   minor haplotype, FD2 mutation, is a bp mutation, where the guanine
CC   nucleotide at bp 2397 (bp 73 of exon 19) is replaced with a cytosine.
CC   This bp mutation causes an arginine to proline missense mutation (R696P)
CC   in the IKBKAP protein, which is predicted to disrupt a potential
CC   phosphorylation site. The IKBKAP nucleic acid sequences are useful for
CC   identifying a subject with FD and for rapid carrier screening. The IKBKAP
CC   gene contains 37 exons and maps to chromosome 9q31. Note: the present
CC   sequence was not shown in the specification, but was derived from the
CC   human wild-type IKBKAP sequence given in Fig 6
XX
SQ   Sequence 66479 BP; 18271 A; 12400 C; 14128 G; 21680 T; 0 U; 0 Other;

  Query Match             97.3%;  Score 14.6;  DB 6;  Length 66479;
  Best Local Similarity   93.3%;  Pred. No. 1.7e+02;
  Matches   14;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GGTTCACSGATTGTC 15
              |||||||:|||||||
Db      33707 GGTTCACCGATTGTC 33721


RESULT 16
ABQ80565
ID   ABQ80565 standard; DNA; 66479 BP.
XX
AC   ABQ80565;
XX
DT   08-NOV-2002  (first entry)
XX
DE   Human IKBKAP wild-type gene.
```

XX
KW Human; IKBKAP; Familial Dysautonomia; FD; Riley-Day syndrome;
KW Hereditary Sensory and Autonomic Neuropathy Type III; carrier screening;
KW gene; chromosome 9q31; ds.
XX
OS Homo sapiens.
XX
PN WO200259381-A2.
XX
PD 01-AUG-2002.
XX
PF 07-JAN-2002; 2002WO-US000473.
XX
PR 06-JAN-2001; 2001US-0260080P.
XX
PA (GEHO) GEN HOSPITAL CORP.
XX
PI Slaugenhaupt S, Gusella JF;
XX
DR WPI; 2002-674806/72.
XX
PT New IKBKAP genes with mutations, useful for identifying a subject with
PT familial dysautonomia (FD), or for rapid carrier screening in the
PT Ashkenazi Jewish population, e.g. screening presymptomatic homozygotes or
PT prenatal diagnosis.
XX
PS Claim 1; Fig 6; 109pp; English.
XX
CC The present invention relates to methods and compositions useful for
CC detecting mutations which cause Familial Dysautonomia (FD, Riley-Day
CC syndrome, Hereditary Sensory and Autonomic Neuropathy Type III) [OMIM
CC 223900]. It was found that mutations in the IKBKAP gene (the present
CC sequence) are associated with FD. The mutation associated with the major
CC haplotype of FD, FD1 mutation, is a base pair (bp) mutation, where the
CC thymine nucleotide located at bp 6 of intron 20 in the IKBKAP gene is
CC replaced with a cytosine. This results in skipping of exon 20 in the mRNA
CC from FD patients, although they continue to express varying levels of
CC wild-type message in a tissue-specific manner. The mutation associated
CC with the minor haplotype, FD2 mutation, is a bp mutation, where the
CC guanine nucleotide at bp 2397 (bp 73 of exon 19) is replaced with a
CC cytosine. This bp mutation causes an arginine to proline missense
CC mutation (R696P) in the IKBKAP protein, which is predicted to disrupt a
CC potential phosphorylation site. The IKBKAP nucleic acid sequences are
CC useful for identifying a subject with FD and for rapid carrier screening.
CC The IKBKAP gene contains 37 exons and maps to chromosome 9q31
XX
SQ Sequence 66479 BP; 18271 A; 12398 C; 14129 G; 21681 T; 0 U; 0 Other;

Query Match 97.3%; Score 14.6; DB 6; Length 66479;
Best Local Similarity 93.3%; Pred. No. 1.7e+02;
Matches 14; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 GGTTCACSGATTGTC 15
||||||:|||||||
Db 33707 GGTTCACGGATTGTC 33721

RESULT 17
ACF67648
ID ACF67648 standard; DNA; 1329 BP.
XX
AC ACF67648;
XX
DT 20-NOV-2003 (first entry)
XX
DE Photorhabdus luminescens nucleotide sequence #6115.
XX
KW Antibacterial; fungicide; insecticide; polymorphism; genetic analysis;
KW detection; food; gene expression; plant; animal; microorganism; toxin;
KW antibiotic; biopesticide; virulence factor; disease model; plague;
KW whooping cough; gene; ds.
XX
OS Photorhabdus luminescens.
XX
PN WO200294867-A2.
XX
PD 28-NOV-2002.
XX
PF 07-FEB-2002; 2002WO-IB003040.
XX
PR 07-FEB-2001; 2001FR-00001659.
XX
PA (INSP) INST PASTEUR.
PA (CNRS) CNRS CENT NAT RECH SCI.
XX
PI Duchaud E, Taourit S, Glaser P, Frangeul L, Kunst F, Danchin A;
PI Buchrieser C;
XX
DR WPI; 2003-148459/14.
XX
PT Genomic sequence of Photorhabdus luminescens and encoded polypeptides,
PT useful e.g. as therapeutic antimicrobials and agricultural pesticides.
XX
PS Claim 2; SEQ ID NO 6115; 1205pp; French.
XX
CC The invention relates to the isolation of genes and their encoded
CC proteins from Photorhabdus luminescens. The isolated sequences are
CC sources of probes and primers for detecting the genome of P. luminescens
CC and related species; to study polymorphisms; for gene analysis and for
CC detection/amplification of the genes. Antibodies (Ab) raised against the
CC polypeptides encoded by the genes are used for detection/identification
CC of P. luminescens, e.g. in foods. The genes, proteins, Ab and cells that
CC carry a gene-containing vector are used to select compounds that
CC modulate, regulate, induce or inhibit expression of the genes in plants,
CC animals or microorganisms other than P. luminescens and are able to alter
CC response or sensitivity to toxins and antibiotics produced by P.
CC luminescens. Cells transformed to express the genes are useful for
CC recombinant production of the proteins, particularly toxins and
CC antibacterials useful as insecticides, bactericides and fungicides. The
CC genes, proteins, vectors containing the genes and Ab are also useful
CC therapeutically (to treat microbial infection by bacteria or fungi that
CC are sensitive to P. luminescens-encoded toxins or antibiotics) and as
CC biopesticides. Other uses of the genes and the proteins are as virulence
CC factors and for identifying targets of human diseases for which P.
CC luminescens is a model (particularly plague and whooping cough). This
CC sequence represents one of the isolated P. luminescens genes
XX
SQ Sequence 1329 BP; 332 A; 340 C; 256 G; 401 T; 0 U; 0 Other;

Query Match 90.7%; Score 13.6; DB 10; Length 1329;
Best Local Similarity 92.9%; Pred. No. 4.9e+02;
Matches 13; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 GGTTCACSGATTGT 14
|||||||:||||||
Db 1000 GGTTCACCGATTGT 1013

RESULT 18
ACF69565
ID ACF69565 standard; DNA; 1920 BP.
XX
AC ACF69565;
XX
DT 20-NOV-2003 (first entry)
XX
DE Photorhabdus luminescens nucleotide sequence #8032.
XX
KW Antibacterial; fungicide; insecticide; polymorphism; genetic analysis;
KW detection; food; gene expression; plant; animal; microorganism; toxin;
KW antibiotic; biopesticide; virulence factor; disease model; plague;
KW whooping cough; gene; ds.
XX
OS Photorhabdus luminescens.
XX
PN WO200294867-A2.

XX
PD 28-NOV-2002.
XX
PF 07-FEB-2002; 2002WO-IB003040.
XX
PR 07-FEB-2001; 2001FR-00001659.
XX
PA (INSP) INST PASTEUR.
PA (CNRS) CNRS CENT NAT RECH SCI.
XX
PI Duchaud E, Taourit S, Glaser P, Frangeul L, Kunst F, Danchin A;
PI Buchrieser C;
XX
DR WPI; 2003-148459/14.
XX
PT Genomic sequence of Photorhabdus luminescens and encoded polypeptides,
PT useful e.g. as therapeutic antimicrobials and agricultural pesticides.
XX
PS Claim 2; SEQ ID NO 8032; 1205pp; French.
XX
CC The invention relates to the isolation of genes and their encoded
CC proteins from Photorhabdus luminescens. The isolated sequences are
CC sources of probes and primers for detecting the genome of P. luminescens
CC and related species; to study polymorphisms; for gene analysis and for
CC detection/amplification of the genes. Antibodies (Ab) raised against the
CC polypeptides encoded by the genes are used for detection/identification
CC of P. luminescens, e.g. in foods. The genes, proteins, Ab and cells that
CC carry a gene-containing vector are used to select compounds that
CC modulate, regulate, induce or inhibit expression of the genes in plants,
CC animals or microorganisms other than P. luminescens and are able to alter
CC response or sensitivity to toxins and antibiotics produced by P.
CC luminescens. Cells transformed to express the genes are useful for
CC recombinant production of the proteins, particularly toxins and
CC antibacterials useful as insecticides, bactericides and fungicides. The
CC genes, proteins, vectors containing the genes and Ab are also useful
CC therapeutically (to treat microbial infection by bacteria or fungi that
CC are sensitive to P. luminescens-encoded toxins or antibiotics) and as
CC biopesticides. Other uses of the genes and the proteins are as virulence
CC factors and for identifying targets of human diseases for which P.
CC luminescens is a model (particularly plague and whooping cough). This
CC sequence represents one of the isolated P. luminescens genes
XX
SQ Sequence 1920 BP; 533 A; 382 C; 456 G; 549 T; 0 U; 0 Other;

Query Match 90.7%; Score 13.6; DB 10; Length 1920;
Best Local Similarity 92.9%; Pred. No. 5e+02;
Matches 13; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 2 GTTCACSGATTGTC 15
||||||:|||||||
Db 476 GTTCACCGATTGTC 489

RESULT 19
ABL15715
ID ABL15715 standard; cDNA; 3770 BP.
XX
AC ABL15715;
XX
DT 26-MAR-2002 (first entry)
XX
DE Drosophila melanogaster expressed polynucleotide SEQ ID NO 41627.
XX
KW Drosophila; developmental biology; cell signalling; insecticide;
KW pharmaceutical; gene; ss.
XX
OS Drosophila melanogaster.
XX
PN WO200171042-A2.
XX
PD 27-SEP-2001.
XX
PF 23-MAR-2001; 2001WO-US009231.
XX
PR 23-MAR-2000; 2000US-0191637P.
PR 11-JUL-2000; 2000US-00614150.
XX
PA (PEKE) PE CORP NY.
XX
PI Venter JC, Adams M, Li PWD, Myers EW;
XX
DR WPI; 2001-656860/75.
DR P-PSDB; ABB71612.
XX
PT New isolated nucleic acid detection reagent for detecting 1000 or more
PT genes from Drosophila and for elucidating cell signaling and cell-cell
PT interactions.
XX
PS Claim 1; SEQ ID NO 41627; 21pp + Sequence Listing; English.
XX
CC The invention relates to an isolated nucleic acid detection reagent
CC capable of detecting 1000 or more genes from Drosophila. The invention is
CC useful in developmental biology and in elucidating cell signalling and
CC cell-cell interactions in higher eukaryotes for the development of
CC insecticides, therapeutics and pharmaceutical drugs. The invention
CC discloses genomic DNA sequences (ABL16176-ABL30511), expressed DNA
CC sequences (ABL01840-ABL16175) and the encoded proteins (ABB57737-
CC ABB72072). The sequence data for this patent did not form part of the
CC printed specification, but was obtained in electronic format directly
CC from WIPO at ftp.wipo.int/pub/published_pct_sequences
XX
SQ Sequence 3770 BP; 990 A; 992 C; 968 G; 820 T; 0 U; 0 Other;

Query Match 90.7%; Score 13.6; DB 4; Length 3770;
Best Local Similarity 92.9%; Pred. No. 5.3e+02;
Matches 13; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 2 GTTCACSGATTGTC 15
||||||:|||||||
Db 1364 GTTCACCGATTGTC 1377

RESULT 20
ABL15714/c
ID ABL15714 standard; cDNA; 10360 BP.
XX
AC ABL15714;
XX
DT 26-MAR-2002 (first entry)
XX
DE Drosophila melanogaster expressed polynucleotide SEQ ID NO 41624.
XX
KW Drosophila; developmental biology; cell signalling; insecticide;
KW pharmaceutical; gene; ss.
XX
OS Drosophila melanogaster.
XX
PN WO200171042-A2.
XX
PD 27-SEP-2001.
XX
PF 23-MAR-2001; 2001WO-US009231.
XX
PR 23-MAR-2000; 2000US-0191637P.
PR 11-JUL-2000; 2000US-00614150.
XX
PA (PEKE) PE CORP NY.
XX
PI Venter JC, Adams M, Li PWD, Myers EW;
XX
DR WPI; 2001-656860/75.
DR P-PSDB; ABB71611.
XX
PT New isolated nucleic acid detection reagent for detecting 1000 or more
PT genes from Drosophila and for elucidating cell signaling and cell-cell
PT interactions.